

# DANSKE KRÆFTFORSKNINGSDAGE

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## ABSTRACT BOOK



Danish Comprehensive Cancer Center

DANSKE MULTIDISCIPLINÆRE CANCER GRUPPER



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**Clinical trials +  
Organisation of treatment:  
Poster #1-51**

**Clinical trials + Organisation of treatment****Abstract title****#1 DAHANCA19: 5-Y update of a randomized phase III trial: Primary (Chemo) RT +/- zalutumumab in head and neck cancer (HNSCC)****Presenting author**

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**Abstract***Aim*

This study aimed to evaluate if concurrent treatment with the EGFR-I zalutumumab during chemo-RT (C-RT) or RT improved outcome in patients with HNSCC.

*Material and Methods*

619 pts entered the study from Nov 2007 to June 2012. The majority of tumors were of oropharyngeal origin (69%). Patients were randomized to control-arm or zalutumumab-arm. The control-arm was primary accelerated RT, predominantly 66-68Gy, 2Gy/tx, 6tx/wk and concomitant daily nimorazole. Stage III-IV carcinomas received weekly cisplatin 40 mg/m<sup>2</sup> during RT. The zalutumumab-arm was identical with the control-arm plus zalutumumab 8 mg/kg. Analyses were performed as intention-to-treat. Primary endpoint was Loco-Regional Control (LRC). Secondary endpoints were Disease Specific Survival (DSS) and Overall Survival (OS).

*Results*

Median observation time was 59 months. 307 pts were in the control-arm and 301 in the zalutumumab-arm. Patient and tumor parameters were well balanced. The 5-year LRC rate was 70% in the zalutumumab-arm vs. 74% in the control-arm, HR: 1.10 [95% CI: 0.81-1.50]. This outcome was also reflected in DSS and OS. Treatment was generally well tolerated, but 94% of the pts in the zalutumumab-arm experienced a skin-rash, and pts treated with zalutumumab experienced significantly more frequent confluent mucositis (70% vs. 56%, p=0.001) and grade 3+4 in-field skin reaction (27% vs. 4%, p<0.0001). The 5-year update did not reveal any significant increase in late morbidity between the arms: severe dysphagia (19% vs. 16%), severe dryness of the mouth (20% vs. 18%), severe late oedema (3% vs. 5%), severe atrophy (8% vs. 6%) and severe fibrosis (20% vs. 16%).

*Conclusion*

Zalutumumab was generally well tolerated, but the addition of concomitant zalutumumab to primary C-RT or RT and nimorazole for HNSCC did not increase loco-regional control nor disease specific or overall survival at 5 years. Acute toxicities, but not late morbidity, were increased in the zalutumumab-arm.



**Clinical trials + Organisation of treatment****Abstract title****#2 DAHANCA 26: Et fase II multicenter, ublindet, randomiseret studie med paclitaxel og capecitabine vs paclitaxel, capecitabine og cetuximab til behandling af recidiverende og/eller metastatisk planocellulært karcinom i hoved- og halsregionen****Presenting author**

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**Abstract***Introduktion*

Uhelbredeligt tilbagefald af hoved-hals kræft er en alvorlig sygdom hvor halvdelen er døde 7-10 måneder efter diagnose selv hvis de behandles med kemoterapi. Sygdommen giver mange symptomer, typisk fra hoved-hals området således at patienterne har smerter, lugter, ændrer udseende og har problemer med vejrtrækning, spising og sanser. Kemoterapi med paclitaxel og capecitabine er standardbehandling hvis der ikke kan gives behandling med helbredelse for øje. Cetuximab er et antistof mod EGF-receptoren på cellernes overflade og har relativt få bivirkninger. Formålet med den igangværende undersøgelse er at vurdere om tillæg af cetuximab til første-linje standardbehandling er bedre end standardbehandling alene, vurderet på graden af tumorrespons, progressionsfri overlevelse, total overlevelse, toksicitet og livskvalitet.

*Materiale og metoder*

Patienter med uhelbredelig pladecelle kræft udgået fra mund, svælg og strube kan inkluderes. Studiet er et randomiseret fase II studie med planlagt 98 inkluderede patienter. Patienterne tilbydes standardbehandling med paclitaxel og capecitabine og randomiseres til cetuximab eller ingenting.

*Resultater*

Studiet startede februar 2016 og der er april 2018 inkluderet 18 patienter. Der er til dato ikke konstateret ikke-tolerabel toksicitet. Inklusionen i studiet har været lavere end forventet. Formentlig afslår patienterne indgang i studiet da tillægsbehandling med cetuximab kræver flere fremøder på hospital end standardbehandlingen alene.

*Konklusion*

Den eksperimentelle behandling opleves tolerabel og der er til dato ikke set uventet toksicitet. Studiet fortsætter på kræftcentre i Aalborg, Aarhus, Odense og Herlev.

## Clinical trials + Organisation of treatment

### Abstract title

### **#3 DAHANCA 28A: Fase I-II studie af accelereret hyperfraktioneret strålebehandling, samtidig cisplatin og nimorazol til patienter med stadie III-IV p16 negativ planocellulært karcinom i mund, svælg og strube**

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### Abstract

#### *Introduktion*

En voksende gruppe patienter (pts) med hoved-hals kræft har HPV-relateret kræft og en god prognose. Der findes imidlertid en gruppe pts med lokalt udbredt sygdom og ikke HPV-relateret kræft der fortsat har en dårlig prognose. Denne gruppe har oftest tobaks- og alkohol relateret kræft og tilsvarende tobaks- og alkohol relaterede følgesygdomme. De har ofte svært ved at tåle behandlings-intensivering såfremt dette medfører øget toksicitet. Vi vil evaluere gennemførligheden af intensiveret strålebehandling hos patienter med HPV negativ stadie III-IV planocellulært karcinom i mund, svælg og strube og med varierende grader af følgesygdomme.

#### *Materiale og metoder*

Fra 2013 til 2015 blev 31 pts med lokalt udbredt kræft i mund, svælg og strube inkluderet i Aalborg, Aarhus og Odense. Pts blev behandlet med 76 Gy/56 fx 10f x/uge, nimorazol x2 daglig og samtidig ugentlig lavdosis cisplatin. Analyser blev udført som intention-to-treat. Primær endepunkt var gennemførligheden af behandlingen. Sekundære endepunkter var akut toksicitet, behov for sondeernæring og loco-regional kontrol.

#### *Resultater*

Median opfølgning er 24 måneder. Medianalderen er 61 og 77% var mænd. Alle havde WHO-performance 0-1, 81% røg fortsat under behandling (median 41 pakke-år) og antallet af følgesygdomme varierede fra 0 til 2. Alle havde HPV-negativ, lokalt fremskreden hoved-hals kræft; primært st. IV (90%) svælg karcinom (74%). 94% gennemførte strålebehandling. Tre års overlevelsen er 61% og sygdomsspecifik overlevelse 73%, mens loco-regionale kontrol er 67%. Næsten 80% havde brug for sondeernæring under behandlingen, men var efter 6 måneder reduceret til 17%. Ved behandlingens afslutning oplevede 20% grad 3 synkebesvær og 15% grad 3 mucositis.

#### *Konklusion*

Accelereret hyperfraktioneret strålebehandling med lavdosis cisplatin og nimorazol er mulig hos pts med lokal udbredt p16-negativ hoved-hals kræft, og resultatet efter tre år er med acceptabel loco-regional kontrol og akut toksicitet.

**Clinical trials + Organisation of treatment****Abstract title****#4 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****Presenting author**

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On behalf of DAHANCA**Abstract***Introduction*

Hypoxic cancer cells within a tumor could be a possible marker of recurrence, as they have shown to be particularly resistant to radiation induced DNA damage and cellular destruction. One way to target this issue could be to increase the dose given to the tumor.

The main purpose of the study is to demonstrate improved curability of radiotherapy in locally advanced HNSCC patients identified by hypoxic FAZA-PET/CT scans.

*Methods*

The study is an open, prospective, experimental single-arm, phase II multi-center study with a planned inclusion of approximately 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 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/CT scan is carried out as part of radiotherapy planning. If hypoxia is visualized, the patient undergoes dose escalated, intensified radiotherapy with HART, nimorazole and weekly cisplatin.

The primary endpoint of the study is loco-regional failure defined as persistent or recurrent disease in the tumor or regional lymph nodes. No salvage surgery (e.g. neck dissection) is allowed. Secondary outcome measures are: overall survival, disease-specific death, acute radiation related morbidity, late radiation related morbidity.

*Preliminary results*

As per May 1st 2018, a total of 15 patients are enrolled and a hypoxic sub-volume is identified within tumors of 73% patients.

Patient recruitment in centers Odense and Aalborg is about to commence.

*Trial registration*

Registered on ClinicalTrials.gov with Identifier NCT02976051.

**Clinical trials + Organisation of treatment****Abstract title****#5 DAHANCA 30: Et randomiseret non-inferiority studie af hypoxi-profilvejledt nimorazolbehandling i forbindelse med primær strålebehandling af planocellulære hoved-halskarcinomer****Presenting author**

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**Abstract***Introduktion*

Tumorhypoxi er årsag til stråleresistens og dårligere outcome ved behandling af kræftkuder i hoved-halsregionen med stråleterapi. Nimorazol er en hypoxisk radiosensitizer, som er vist at reducere stråleresistensen og dermed forbedre stråleeffekten i iltfattige kræftkuder. Nimorazol gives i dag til næsten alle strålebehandlede patienter med hoved-halskræft, velvidende at det formentlig kun er virksomt hos de mest ilt-fattige svulster. Hidtil har man ikke været i stand til særskilt at adskille ilt-fattige fra ilt-rige svulster. Med en udviklet hypoxi gen-profil tyder det på, at det er muligt at udpege de ilt-rige svulster, hvor nimorazol ikke har væsentlig betydning. Ved at undlade brug af nimorazol hos denne gruppe, kan disse patienter spares for bivirkninger til præparatet. Formålet med undersøgelsen er, at eftervise, hvorvidt hypoxi gen-profilen kan udpege patienter som ikke har gavn af nimorazol under strålebehandling.

*Materiale og metoder*

Patienter med planocellulær hoved-halskarcinom, hvor der i henhold til DAHANCA's retningslinjer er indikation for hypoxisk modifikation med nimorazol under primær strålebehandling kan inkluderes. Studiet er et randomiseret non-inferiority studie med planlagt 1262 inkluderede og randomiserede patienter. Hos inkluderede patienter laves hypoxisk profil på deres diagnostiske biopsi. Hvis denne tyder på en ilt-rig kræftkude, randomiseres til stråleterapi/kemostråleterapi +/- nimorazol. Hvis hypoxi-profilen tyder på en ilt-fattig kræftkude får patienten standard stråleterapi/kemostråleterapi (incl. nimorazol).

*Resultater*

Studiet startede inklusion i aug 2016 og ultimo april 2018 er der 228 inkluderede patienter, hvoraf 150 er randomiserede. Inklusionen i studiet har været lavere end forventet. Dette skyldes formentlig at enkelte nationale onkologiske centre endnu ikke er initieret. Studiet forventes dog snart initieret også på Rigshospitalet og Næstved Sygehus.

**Clinical trials + Organisation of treatment****Abstract title****#6 DAHANCA 27: Transoral laser assisted microsurgery for T1a glottic cancer****Presenting author**

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**Abstract***Introduction*

Glottic cancer is, in Denmark, currently treated with accelerated radiotherapy (RT). The treatment is efficient and 5 years primary control is 95% for patients with T1aN0M0 glottic cancer. Control with salvage is 98%. Modern technology has made it possible to surgically remove the tumour by transoral laser assisted microsurgery (TLM). This treatment is faster, of less strain to the patient and probably cheaper. Unfortunately it is unknown if cancer control and treatment morbidity are comparable in TLM and RT.

*Aim*

The aim is to investigate whether TLM is non-inferior compared to accelerated RT in treating patients with T1aN0M0 glottic cancer.

*Materials and methodology*

In total 3 patients operated radically with TLM were prospectively included in this national study. Patients will be followed for five years. Voice quality will be evaluated at 6 month and 3 years of follow up. The primary end point is laryngectomy free survival. Secondary endpoints include primary control, control with salvage, survival, voice outcome, and costs. Data on TLM treated patients will be compared to a national historic cohort of 350 RT treated patients prospectively recorded in the DAHANCA-database.

*Perspective*

By comparing national cohorts of consecutive patients treated with TLM and RT respectively we will avoid selection bias. This study will provide better evidence of the value of TLM vs. RT compared to existing data. Outcome of this study will underlie the decision on whether to implement TLM as a standard treatment for T1a glottis cancer in Denmark.

## Clinical trials + Organisation of treatment

### Abstract title

#### **#7 DAHANCA 34 (QoLATI studiet): Et nationalt randomiseret forsøg med robotoperation versus strålebehandling til patienter med tidlige stadier af mundsvælgkræft**

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### Abstract

#### *Introduktion*

Antallet af patienter med mundsvælgkræft (mandler og tungerod) er stigende i Danmark, og det forventes at antallet af nye tilfælde i de kommende år vil stige til ca. 400 patienter/år. Standardbehandlingen af mundsvælgkræft i Danmark er strålebehandling med eller uden kemoterapi. Denne behandling er ofte effektiv, men giver hyppigt bivirkninger både på kort og lang sigt. I de seneste år er der fremkommet en ny behandling til tidlige stadier bestående af robotassisteret operation via mundhulen (Transoral robotkirurgi, TORS). Flere mindre forsøg fra udlandet tyder på at overlevelsen efter TORS eller strålebehandling er ligeværdig, og forhåbningen er at patienter behandlet med TORS vil have færre senfølger. Der findes ingen direkte sammenligning af de to behandlingsmetoder, og vi vil derfor gennemføre en national randomiseret undersøgelse for at afklare om TORS reducerer forekomsten af senfølger sammenlignet med strålebehandling.

#### *Materiale og metoder*

Danske patienter med tidlig stadium mundsvælgkræft, der vurderes operable tilbydes at indgå i undersøgelsen. Hvis de indvilger, vil der blive trukket lod imellem operation og strålebehandling, i forholdet 2:1. Ved ikke radikal operation vil de kirurgiske patienter blive tilbudt post-operativ strålebehandling. Alle patienter vil før, under og efter behandlingerne gennemgå en række undersøgelser med fokus på synkefunktion og livskvalitet.

#### *Resultater*

Operation kan foretages i København (Rigshospitalet), Århus og Odense, mens strålebehandling kan foretages i København (Rigshospitalet/Herlev), Næstved, Odense, Århus og Aalborg. Hovedendepunktet vil være synke-relateret livskvalitet 12 måneder efter behandling, men undersøgelsen vil også sammenligne overlevelse, tilbagefald, synkefunktion og kontakt til arbejdsmarkedet.

#### *Konklusion*

Med undersøgelsen håber vi at kunne bidrage med evidens for om TORS ved tidlig stadium mundsvælgkræft er forbundet med færre bivirkninger sammenlignet med primær strålebehandling.

**Clinical trials + Organisation of treatment****Abstract title****#8 DAHANCA 35: Et nationalt randomiseret forsøg med strålebehandling med enten fotoner eller protoner til patienter med hoved-halskræft****Presenting author**

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**Abstract***Introduktion*

Med åbningen af Dansk Center for Partikelterapi (DCPT), bliver der mulighed for at tilbyde patienter protonbehandling i Danmark. Bivirkninger efter strålebehandling for svælg og strubekræft er hyppige og alvorlige. Flere matematiske modeller for bivirkningerne er publiceret for konventionel foton-strålebehandling. Det er usikkert, hvorvidt modellerne kan overføres til proton-strålebehandling. Samtidig er der usikkerheder i forbindelse med planlægning og afgivelse af protonterapi, hvilket kan udgøre et reelt klinisk problem.

*Materiale og metoder*

Patienter med kræft i svælg og strube i Danmark, egnede til strålebehandling, får lavet en computerbaseret sammenligning mellem den konventionelle foton- og proton behandling. Ved forventet betydelig reduktion i risikoen for bivirkninger med protonterapi frem for fotonterapi, tilbydes patienterne lodtrækning til enten protonbehandling på DCPT eller fotonterapi på lokalt center. Patienterne får før og efter behandlingen undersøgt synkefunktion, stimuleret spytmåling og livskvalitetsmålinger (spørgeskemaer). Efter afsluttet strålebehandling følges alle patienterne på lokalt center.

*Resultater*

Alle danske centre, der behandler patienter med hoved-halskræft, deltager. Udvælgelseskriterier og retningslinjer for planlægning med protonterapi er ved at blive udarbejdet således at de sammenlignende stråleplaner kan laves lokalt på alle centre.

*Konklusion*

Med undersøgelsen forventer vi at kunne skaffe evidens for, hvilke patienter med hoved-halskræft, der har gavn af proton strålebehandling. Ved at inkludere patienter, der teoretisk har gavn af protonterapi, vil vi også undersøge modellernes og de sammenlignende dosisplaners potentiale til at udvælge patienter. Håbet er, at data også kan indgå i større datamaterialer via EPTN (European Particle Therapy Network) så vi kan få statistisk styrke til at detektere evt. forskelle i tumorkontrol.

## Clinical trials + Organisation of treatment

### Abstract title

#### **#9 DAHANCA 21: Et internationalt multicenter randomiseret forsøg vedrørende effekten af tryk-kammerbehandling (hyperbar ilt - HBO) på stråleinduceret vævsdød (osteoradionekrose - ORN) af underkæbens knoglevæv**

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### Abstract

#### *Indroduktion*

Stråleinduceret vævsdød af knoglevæv i underkæben (osteoradionekrose - ORN) er en alvorlig komplikation til strålebehandling af hoved-halskræft, ofte med funktionstab ifm. opera-tiv fjernelse af dødt knoglevæv og tænder. HBO er siden 1960'erne anvendt til behandling af ORN. Tilførsel af ilt under tryk svarende til dykning på 14-15 meter medfører, at ilt optages i forøgede koncentrationer i vævet, hvorefter nydannelsen af blodkar stimuleres, og blodforsyningen bedres. Imidlertid mangler der evidens for en klinisk effekt heraf. Formålet med forsøget er at afklare, hvorvidt HBO som supplement til operation har en effekt på stråleskade i underkæbens knogle-væv.

#### *Materiale og metoder*

Forsøget har sit center i København, de øvrige centre er Liverpool, Leeds, Wales, South Coast, London, Bradford og Göteborg. Pt. henvist til kæbekirurgisk resektion for ORN er randomiseret til 1) kirurgisk behandling alene eller 2) kirurgisk behandling forudgået af 30 og efterfulgt af 10 HBO-behandlinger. Hver behandling indebærer tilførsel af 100% ilt i en hætte med tryksætning til 2.4 ATA (24 meters dykning) i et flerpersonerskammer. Udover sygdomsfrihed (ingen knoglelæsion eller radiologiske tegn ORN) 1 år efter fjernelse af ORN, registreres effektmål som smerte og livskvalitet.

#### *Resultater*

77 personer er rekrutteret til forsøget. 21 er faldet fra pga. død, ny cancer/recidiv eller manglende compliance. 36 er randomiseret til HBO, 41 til kirurgisk behandling alene. Af de 42 gennemførte forløb på nuværende tidspunkt er 10/16 sygdomsfri 1 år efter kirurgi og HBO (63%) og 10/26 (38%) efter kirurgi uden HBO.

#### *Konklusion*

Da forsøget stadig er i gang, er der endnu ikke gennemført statistisk analyse. De foreløbige resultater viser, at næsten 2/3 af de, som modtog trykkammerbehandling som supplement til kirurgi, var sygdomsfri efter 1 år i modsætning til kun 1/3 af deltagerne i gruppen med kirurgi alene. Det tyder således på, at der er en vis effekt af trykkammerbehandlingen.



**Clinical trials + Organisation of treatment****Abstract title****#10 The DBCG RT HYPO trial: Hypo- vs normofractionated radiation therapy of early stage breast cancer in 1882 patients included in a clinically controlled randomized trial****Presenting author**

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**Abstract***Introduction*

Based on poor results using hypofractionated (hypo) adjuvant radiotherapy (RT) of breast cancer (BC) 50 Gy/25 fr. has been Danish Breast Cancer Group (DBCG) standard since 1982. Results from the UK and Canada stimulated a renewed interest in hypo, and the non-inferiority DBCG HYPO trial was initiated. The hypothesis was that 40 Gy/15 fr does not result in more grade 2-3 breast induration than 50 Gy/25 fr 3 years post RT.

*Material/Methods*

From 2009-2014, 1882 patients >40 years operated with breast conservation for pT1-2 pN0-1(mic) BC (n=1617) or DCIS (n=251) were randomized 50 Gy vs. 40Gy. Strata were institution, breast size, chemotherapy(CT) and boost. The primary endpoint was grade 2-3 induration 3 years post RT, secondary endpoints were other late effects, genetic risk profile for fibrosis and recurrences. ClinicalTrial NCT00909818.

*Results*

942 pts (50.4%) were assigned to 50 Gy and 926 (49.6%) to 40 Gy. Median age was 59 years. Median follow up was 5 years. Results are actuarial 3- and 5-year rates using morbidity in 1831 pts for univariate and 1494 pts for multivariate analysis. Induration at 3 and 5 years was seen in 14% and 16% of the pts (50 Gy), and in 11% and 12% of the pts (40 Gy), HR (40 Gy vs 50 Gy) 0.73 (0.57-0.95). Comparing induration in small (48%) vs large (52%) breasts the HR was 1.43 (1.10-1.86). CT (36%) did not increase induration, HR 0.99 (0.76-1.29). Boost was given to 15% and the boost vs no boost HR was 1.62 (1.21-2.13). Current smokers (20%) vs never/previous smokers developed more induration, HR 1.60 (1.21-2.13). Multivariate analysis identified 50 Gy, large breasts, boost and current smoker as independent risk factors. In the 50 Gy / 40 Gy group loco-regional recurrence was reported in 11 pts / 8 pts.

*Conclusion*

Hypo breast RT does not result in more induration compared to normo RT. Large breast size, boost and smoking are independent risk factors for induration. The 5 yr loco-regional recurrence risk is very low.

**Clinical trials + Organisation of treatment****Abstract title****#11 The DBCG RT Skagen Trial 1: Hypo- vs normofractionated loco-regional radiation therapy of early stage breast cancer in a clinically controlled randomized trial****Presenting author**

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**Abstract***Introduction*

Based on poor results using hypofractionated radiotherapy (RT) of breast cancer (BC) 50 Gy/25 fr. has been Danish Breast Cancer Group (DBCG) standard for loco-regional therapy since 1982. Results from the DBCG HYPO trial stimulated a renewed interest in hypofractionation, and the DBCG SKAGEN TRIAL 1 was initiated. The hypothesis is that 40 Gy/15 fr does not result in more arm lymph edema than 50 Gy/25 fr at 3 years.

*Material/Methods*

Since 2015, patients  $\geq 18$  years operated for BC with an indication for loco-regional RT are randomized 1:1 to 50 Gy vs. 40Gy. The primary endpoint is ipsilateral arm lymph edema 3 years post RT. Edema is present if the circumference of the arm is 10% higher compared with the other arm. Secondary endpoints are other normal tissue responses, patient reported outcomes and recurrences. The RT planning is based on the ESTRO consensus for target volume delineation, and treatment planning follows the DBCG guidelines. Danish centers submit all treatment plans to the CIRRO National Dose Plan Bank. Non-Danish centers submit some plans for quality assurance (QA) of the planning. It is expected that 10% of patients treated with 50 Gy will have arm lymph oedema 3 years after RT. To rule out an increase by 10% using 40 Gy 1012 patients are needed with 3 years morbidity evaluation. Accrual remains open until 3 years morbidity information has been collected in 1012 patients. ClinicalTrial NCT02384733.

*Results*

The trial is open for accrual in 14 departments in 6 countries, and as of April 2018, 1304 patients are accrued. Extensive QA of the RT planning demonstrates high compliance with DBCG guidelines.

*Conclusion*

It is estimated that the DBCG SKAGEN TRIAL 1 will close with 2700 patients in 2020, thus providing statistical power for analyses of the importance of fractionation in relevant subgroups. The DBCG RT Committee will decide what is the future standard fractionation for loco-regional radiation therapy in 2020.

**Clinical trials + Organisation of treatment****Abstract title****#12 The DBCG RT PBI trial: Accelerated partial breast radiation therapy after breast conservation for early breast cancer, early results from 882 patients enrolled in a clinically controlled randomized trial****Presenting author**

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**Abstract***Introduction*

The risk of local recurrence after radiation therapy (RT) of breast cancer (BC) is now so low that ESTRO and ASTRO have suggested guidelines to select patients who may be safely treated with partial breast (PBI) and not whole breast irradiation (WBI). In the Danish Breast Cancer Group (DBCG) the randomized DBCG PBI trial was initiated to safely introduce PBI as standard in DK.

*Material/Methods*

Patients  $\geq 60$  years operated with breast conservation for non-lobular breast cancer (BC) pT1 pN0, ER+, grade 1 or 2, HER2-, margin  $\geq 2$ mm were enrolled and randomized to PBI vs WBI, all cases based on 40Gy/15 fr. The primary endpoint was grade 2-3 breast induration 3 years after RT, secondary endpoints were other RT morbidities, genetic risk profile for RT-induced fibrosis and recurrences. ClinicalTrial NCT00892814.

*Results*

In 6 RT centers in DK 882 pts were enrolled in 2009-16. At analysis 353 pts (40%) had  $\geq 3$  years follow up. Here 3 year data is reported. Induration was detected in 6.4% in the PBI arm and in 7.7% in the WBI arm (HR 0.76, 95% CI, 0.39-1.47). Comparing the PBI vs the WBI arm there were no differences in dyspigmentation (8.1% vs 11.0%), telangiectasia (5.3% vs 8.9%), edema (0.6% vs 0.6%), scar (21.5% vs 17.1%), and global cosmetic outcome (excellent/good) was 84.3% vs 83.9%. In the PBI / WBI arm local recurrence was reported in 1 pt / 2 pts, regional recurrences 0 pt / 0 pt, distant failure 1 pt / 2 pts, new contralateral BC / DCIS 2 pts / 2 pts and other malignancy 8 pts / 16 pts. One patient had died from BC, 7 from other malignancy, 7 from non-cancer causes.

*Conclusion*

Using 40/15 fr for PBI in selected BC patients results in few late RT induced morbidities with no difference compared with WBI. These results are in harmony with results from the large UK IMPORT LOW trial using the same RT technique. Thus, 40 Gy/15 fr external beam PBI is now DBCG standard for breast RT in patients fulfilling the inclusion criteria for the DBCG PBI trial.

**Clinical trials + Organisation of treatment****Abstract title****#13 The DBCG RT Natural trial: Partial versus no breast radiation therapy for women  $\geq$  60 years operated with breast conservation for a relatively low risk early breast cancer, a clinically controlled randomized trial****Presenting author**

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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 estimated to 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 contralateral new primary. In the DBCG RT Natural trial the DBCG RT Committee wants to test if omission of PBI in selected patients is possible without causing unacceptable more local recurrences.

*Material/Methods*

Patients  $\geq$ 60 years operated with breast conservation for a low risk breast cancer (non-lobular, pT1, pN0, ER+, grade 1-2, HER2-, margin  $\geq$ 2mm) are randomized  $\pm$  PBI, where PBI is based on 3DCRT 40 Gy/15 fr. Strata are institution and endocrine therapy. The study will randomize 1:1, and 600 patients will be accrued. A 5 year local recurrence of 3% is accepted with omission of PBI, thus 1% higher than the risk of new contralateral BC. The primary endpoint is 5-year invasive local recurrence. Secondary endpoints are local morbidity, fear of recurrence and pattern of recurrences. The study is expected to open for accrual in 2018.

*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 + Organisation of treatment****Abstract title****#14 The DBCG RT Proton trial: an initiative to introduce proton therapy for early breast cancer in an evidence-based way in Denmark****Presenting author**

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**Abstract***Introduction*

The prognosis of early breast cancer (BC) has improved over decades, thus long-term morbidities increasingly play a role. Serious late effects from radiation therapy (RT) are second cancer and heart disease. Adjuvant RT significantly improves local and distant control leading to improved survival, but this gain must be balanced with risk of RT induced late effects. Proton therapy (PT) becomes an option for RT of BC in DK in 2018. PT causes good target coverage but lower dose to critical organs at risk and therefore holds potential to reduce the risk of serious late effects. The Danish Breast Cancer Group (DBCG) wants to investigate if PT is an optimal choice for selected BC patients. The aim is to initiate a randomized controlled trial testing photon vs proton RT.

*Material/Methods*

PT has never been offered to BC patients in DK, thus before a randomized trial can be designed, a single-arm prospective cohort study is planned including 100 patients selected on unacceptable high dose to lung and/or heart when irradiated for a high-risk BC. The definition of what is acceptable is investigated in DBCG lead international retrospective study being initiated April 2018 investigating doses to lung and heart in treatment plans with optimal dose coverage of target volumes. When cut-values are defined for acceptable lung/heart dose, every BC patient with too high doses to lung/heart will be referred for PT. The endpoint of the cohort study is feasibility, thus how many patients offered PT accept PT.

*Results*

The retrospective part of the study is open in DK and many centers abroad are invited to participate. Several departments from outside DK have expressed interest in participating in the DBCG RT Proton trial, both the cohort study and the randomized trial.

*Conclusion*

Initial investigations are ongoing in DBCG to prepare an evidence-based introduction of PT in DK to selected BC patients. This takes place in close collaboration with international colleagues.

**Clinical trials + Organisation of treatment****Abstract title****#15 Survival and axillary recurrence following sentinel node- positive breast cancer without completion axillary lymph node dissection – the SENOMAC trial****Presenting author**

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**Abstract**

Sentinel node (SN) biopsy in breast cancer has proven to be reliable and safe staging procedure in clinical node-negative breast cancer. Moreover, SN biopsy alone is associated with significantly less postoperative arm morbidity. The low rate of axillary recurrence after any breast cancer treatment seen these days has questioned the role of ALND even among patients who have SN metastases. Two studies have been published in recent years in which SN-positive breast cancer patients were randomized either to undergo completion ALND or not. In the ACOSOG Z0011 study, which included patients with breast-conserving surgery, the experimental arm did not receive any additional treatment to the axilla. In the AMAROS trial, the experimental arm received radiation therapy (RT) to the axilla. Both trials included both SN micro- and macrometastases, and did not demonstrate any difference in the rate of axillary recurrence or survival. However, especially the Z0011 study had several weaknesses.

The prospective multinational SENOMAC trial includes patients with 1-2 SN macrometastases operated with breast-conserving surgery or mastectomy. Patients are randomized to either undergo ALND or not. Participating countries are allowed to adhere to their respective national adjuvant guidelines meaning that in Denmark, patients in the interventional arm will have full RT to the axilla (level I-III). The primary endpoint is breast cancer-specific survival at five years. SENOMAC is designed as a non-inferiority trial aiming at ruling out a worsening in breast cancer-specific survival in the experimental arm (no ALND) of at most 2.5% after 5 years by including 3500 patients. Secondary endpoints include recurrence rate, Quality of Life, and arm morbidity.

Recruitment for the study started in Denmark in April 2017. As per June 1, 2018, in all 838 patients have been included, of which 116 is from 8 Danish centers. It is expected that within 2018 all Danish breast surgical units will take part in the study.

**Clinical trials + Organisation of treatment****Abstract title****#16 The DBCG RT Recon Trial: Delayed-Immediate versus delayed breast reconstruction in early breast cancer patients treated with mastectomy and adjuvant loco-regional radiotherapy. A multicenter randomized clinical trial****Presenting author**

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**Abstract**

Along with the improving prognosis for breast cancer, more attention has been raised towards better cosmetic outcome, including breast reconstruction. In case of primary reconstruction it is importance to choose the safest technique in order not to delay adjuvant systemic treatment. A proportion of patients treated by mastectomy are recommended post mastectomy radiotherapy (PMRT) which is known to increase complication rate after primary reconstruction. Accordingly secondary reconstruction is often preferred in these patients. In secondary reconstruction it is not possible to preserve the native skin envelope, resulting in a deteriorated cosmetic result. In delayed-immediate reconstruction a skin sparing mastectomy and temporary reconstruction with implant is performed at primary surgery. This preserves the skin envelope while radiation therapy is given, thus improving the result after final secondary reconstruction.

The aim of this study is to compare delayed-immediate breast reconstruction (arm A) to secondary reconstruction (arm B) in breast cancer patients treated by mastectomy and PMRT based on new ESTRO guidelines for target volume delineation and treatment planning, developed as part of the trial. The study is planned as an international randomized trial in collaboration between breast surgeons, plastic surgeons and clinical oncologists. Primary endpoint is complication rate defined as infection, hematoma, loss of implant, necrosis and seroma. Secondary end points are lymphedema, range of movement of the shoulder, timing of adjuvant treatment, recurrence and survival. In addition patient's satisfaction and quality of life will be compared using BREAST-Q survey.

Estimated inclusion is 590 patients over 5 years, with 10 years of follow-up.

If the complication rate after delayed-immediate reconstruction is acceptable, the DBCG may choose to recommend the method for breast cancer patients treated by mastectomy and PMRT who wish a reconstruction.

**Clinical trials + Organisation of treatment****Abstract title****#17 The DBCG RT Recon trial: Consensus on target volume delineation and radiation treatment planning strategy in early breast cancer patients operated with mastectomy and immediate implant-based reconstruction****Presenting author**

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**Abstract***Purpose*

Breast cancer is increasingly treated with mastectomy and immediate reconstruction followed by radiotherapy (RT) despite an increased risk of complication after RT. The Danish Breast Cancer Group (DBCG) is starting a randomized trial to compare delayed-immediate versus delayed reconstruction in relation to time of RT. This work aimed to reach consensus on chest wall target definition and evaluate different RT treatment techniques.

*Methods*

Consensus on chest wall target delineation was reached through email discussion. Two cases with retro-pectoral implant (RPI) had target delineated accordingly. Other volumes followed ESTRO guidelines. The cases were sent to all Danish RT centres and six international centres. All were asked to make plans, using their choice of RT treatment technique but no bolus, prioritizing target coverage but with acceptable organ-at-risk (OAR) dose. Plans and doses were collected and evaluated.

*Results*

In non-locally advanced breast cancer (non-LABC) treated with mastectomy and RPI the CTVp\_consensus is ventral to the implant (subcutaneous lymphatic plexus (S-LP)). In LABC the CTVp\_consensus includes the volume both ventral and dorsal to the implant (both S-LP and pre-pectoral LP). In total 35 dose plans were made. RT techniques included conformal field-in-field (FiF), IMRT, VMAT and tomotherapy (HT). As a rule, inversely optimized (IO) plans (IMRT, VMAT, HT) had better target coverage, especially near the skin, but FiF plans could achieve similar coverage with more subfields. IO plans traded high dose for low dose in ipsilateral OAR. This reduced mean lung dose but increased mean heart dose (MHD) by 1-2 Gy. For the contralateral OAR, IO plans added low dose areas.

*Conclusion*

Consensus on target volume delineation was reached. All RT techniques achieved target coverage, but FiF plans required many subfields. In ipsilateral OAR IO plans traded high dose for low dose and added low dose in the contralateral OAR. MHD was higher in IO plans.



**Clinical trials + Organisation of treatment****Abstract title****#18 Molecular evaluation in metastatic breast cancer – a clinical study of accuracy and response assessment (MESTAR)****Presenting author**

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**Abstract***Background*

Women with metastatic breast cancer (MBC) cannot be cured and need life-long medical treatment in order to prevent growth of their cancer.

It is essential to know the exact baseline stage of MBC in order to allow adequate evaluation of treatment response subsequently.

We have shown recently that FDG-PET/CT has a higher accuracy than conventional imaging with CT and bone scintigraphy when diagnosing MBC.

Response evaluation criteria have traditionally been based on the morphological size of solid tumors but we consider it important to include changes in metabolic activity for evaluation of treatment response, since metabolic changes occur before morphological changes can be detected.

We hypothesize that molecular evaluation with FDG-PET/CT more accurately assess treatment response or failure to breast cancer directed treatments.

*Method*

Part A: All women referred to Odense University Hospital with suspected MBC will be examined with FDG-PET/CT and whole body MRI if bone metastases are detected. Women with suspected metastases on FDG-PET/CT or MRI will have a biopsy from a suitable lesion to confirm the diagnosis.

Part B: All women with biopsy verified MBC will initiate standard medical treatment directed by the biomarker profile of the biopsy. Treatment response will be evaluated by conventional CT criteria and compared to novel criteria according to FDG- PET/CT.

We expect to include 360 patients and have already included 125 patients, of whom 35 patients are diagnosed with MBC and entered the response evaluation part of the project.

Patients are involved in the planning and conduct of the project.\u02028

*Clinical impact*

We hope that patients will benefit in terms of being spared for ineffective toxic treatment due to earlier detection of failure to respond, and hence leading to earlier treatment transition.

**Clinical trials + Organisation of treatment****Abstract title****#19 IMPROVE: Implementing non-invasive circulating tumor DNA analysis to optimize the operative and postoperative treatment for patients with colorectal cancer****Presenting author**

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**Abstract***Introduction*

Patients with early stage colorectal cancer (CRC) have a good chance of survival, however up to 10% of stage I and ~20% of stage II patients will experience relapse. The evidence of benefit of adjuvant chemotherapy (ACT) in stage I and II is not well established.

Analysis of circulating tumor DNA (ctDNA) is an emerging tool that recently demonstrated a strong prognostic value for stage I and II CRC. Post-operative detection of ctDNA identifies patients with the highest risk of recurrence. These patients may potentially benefit from ACT. However, at present it is unclear to what extent ACT can reduce their relapse risk.

*Objective*

The IMPROVE study aims to investigate if ctDNA-based ACT treatment decisions may lead to decreased recurrence rates in stage I and II CRC.

*Materials and methods*

IMPROVE is a national study aiming to recruit 1,800 stage I-III patients over a two year period, starting May 2018. ctDNA analysis will be performed on blood samples longitudinally collected for up to 5 years post-surgery. We expect to identify at least 70 stage I and II patients without an indication for ACT, but ctDNA positive 2-4 weeks after surgery. These high-risk patients will be enrolled in a prospective randomized intervention trial named IMPROVE-IT and randomized to either A) ACT + intensified follow-up or B) intensified follow-up.

*Results*

IMPROVE has just begun recruiting and results are consequently limited. The trial design will be presented and discussed. Pilot ctDNA data from a retrospective analysis of plasma samples from 130 stage I-III CRC patients will be presented. The data confirm that patients ctDNA positive 2-4 weeks after surgery are at high risk of relapsing (HR 8.3, 95%CI 3-23) and show that ACT may eliminate this risk in up to 30% patients, lending support to the feasibility of the IMPROVE study.

*Conclusions*

IMPROVE is the first Danish interventional trial investigating the benefit of using ctDNA in clinical decision making.

**Clinical trials + Organisation of treatment****Abstract title****#20 NORDIC9: A randomized phase II trial comparing full-dose monotherapy (S-1) with dose-reduced combination-therapy (S-1 + oxaliplatin) in older patients with metastatic colorectal cancer (mCRC), who are not candidates for standard combination therapy****Presenting author**

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**Abstract***Introduction*

Colorectal cancer is a disease of older adults, but knowledge on treatment is sparse, as older patients (pts) are underrepresented in clinical trials. Here we present data on toxicity from the NORDIC9 trial.

*Method*

NORDIC9 explored treatment of older mCRC pts ( $\geq 70$  years) who were not candidates for full-dose combination therapy. Pts were randomized to full-dose monotherapy (Arm A: S-1 30 mg/m<sup>2</sup> po bid d 1-14 q3w, followed by irinotecan upon progression) or reduced dose (80%) combination therapy (Arm B: S-1 20 mg/m<sup>2</sup> po bid d 1-14 + oxaliplatin 100 mg/m<sup>2</sup> iv d 1 q3w, followed by S-1 + irinotecan q3w). Addition of bevacizumab (7.5 mg/kg iv d 1) was optional. Geriatric screening tools (G-8, VES-13, handgrip strength, Timed-Up-and-Go), Charlson Comorbidity Index and QoL were evaluated at baseline. Blood samples and tumor tissue were prospectively collected. Primary endpoint is PFS. Secondary endpoints are response rate, survival and correlations between screening tools and efficacy and safety.

*Results*

156 eligible pts were randomized from March 2015 to October 2017. Median age was 78 years (range 70-88), 51% was male, 44% was in performance status (PS) 1, 17% in PS 2. 32% received bevacizumab. Baseline characteristics were equally distributed in the two arms. Grade 3-4 toxicity was fatigue (8%), diarrhea (7%), nausea (3%) vomiting (3%), neuropathy (4%), cardiotoxicity (0.6%). No grade 3-4 febrile neutropenia or hand-foot-syndrome was seen. The preplanned safety analysis showed an increased incidence of grade 3-4 diarrhea in pts with GFR <70 ml/min, however this was not recovered in the final data set. 13 pts discontinued treatment after 1 cycle due to toxicity (n=8) or PD/clinical deterioration (n=5). PFS, RR and OS are pending. We are looking for prognostic and predictive markers which will be presented at the meeting.

*Conclusion*

Prospective trials are feasible in older patients with mCRC. Treatment was well tolerated with no unexpected toxicities.

**Clinical trials + Organisation of treatment****Abstract title****#21 Calcium electroporation for the treatment of colorectal cancer (Calcium EndoVe)****Presenting author**

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**Authors**

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**Abstract***Aim*

The aim of this phase I clinical trial is to establish safety and efficacy of calcium electroporation for colorectal cancer.

*Background*

Electroporation is a method used to permeabilize cell membranes with high voltage pulses, allowing flow of otherwise poorly or non-permeating substances such as calcium into the cell. Recent studies have shown that calcium electroporation efficiently eliminates cancer cells, and furthermore, potentially initiates a favorable systemic immunologic response. Additionally, studies show that cancer cells are vulnerable to the treatment, whereas normal cells are more resistant to calcium electroporation.

*Study design*

A total of 6 patients with inoperable colorectal cancer will be included. All patients will have been offered the standard of care and all available alternatives before entering the protocol. All patients will be treated once, but in case of residual tumor tissue at follow-up, they will be offered re-treatment. A maximum of 3 treatments per patient will be conducted with an interval of minimum 4 weeks. The patients will be followed with regular examinations for up to 12 months. Intraluminal biopsies from the tumor will be collected just before the treatment and at follow-up. Tissue will be characterized and compared regarding standard histology and immune invasion. Additionally, blood samples will be collected. Systemic immunological response will be analysed. Furthermore, circulating levels of ctDNA and cfDNA will be measured. Finally, patients are followed with CT/MR scans. Primary tumor and metastases will be evaluated according to RECIST-criteria.

*Study treatment*

Calcium chloride (9 mg/ml) will be injected into the tumor before the electrical pulses are delivered. The electrical pulses will be delivered in a series of eight wave pulses of 100 µsec, 1 Hz, 1000 v/cm. The endoscopic device (EndoVE) is designed as a single-use, vacuum assisted electrode attachment for a standard endoscope.

**Clinical trials + Organisation of treatment****Abstract title****#22 Introducing minimal invasive oesophagectomy in a multi-disciplinary tertiary referral centre****Presenting author**

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**Abstract***Background*

Minimal invasive oesophagectomy (MIO) in cancer patients has gained increasing popularity over the past 5 years because of reduced blood loss, lower total morbidity and respiratory complications, and a long term survival at least equivalent to the results after open resection. This study reports the results of the first two years after introducing MIO within the frames of a multi-disciplinary setting at Odense University Hospital.

*Material and methods*

All MIO procedures were prospectively registered in a database, and the patients were followed until death, 2 years after surgery, or the end of the inclusion period.

*Results*

One-hundred-and-forty procedures were performed between November 2015 and February 2018. There were 19 women and 121 men with a median age of 67 years (range 16-83 years). Patients were divided into the first 70 patients and the last 70 patients. The mean procedure time was 352 minutes for the "first patients" and 331 minutes for the "last patients" ( $p < 0.001$ ). The risk of conversion to open surgery in the abdominal procedure was 6% for the "first patients" and 9% for the "last patients" (NS). For the thoracic procedure the corresponding figures were 11% and 6% (NS), respectively. The median length of postoperative stay was 9 days for both groups. The risk of anastomotic leakage was 16% ("first patients") and 11% ("last patients") (NS). However, endoscopic or surgical treatment was required in only 4% and 7%, respectively. For all 140 patients, pulmonary complications were observed in 26 cases (18%) and cardiac complications were registered in 15 cases (11%). The 30 day mortality rate was 3% and the 1 year survival rate was 83%.

*Conclusions*

MIO can be introduced in a multi-disciplinary tertiary referral center with short time outcomes at least comparable to open resection. More leakages treated conservatively, fewer pulmonary complications and early discharge are some of the potential benefits of the MIO approach.

**Clinical trials + Organisation of treatment****Abstract title****#23 Impact of chemo and radiation therapy on left ventricular systolic and diastolic function in patients with cancer in esophagus and gastroesophageal junction - a prospective study design****Presenting author**

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**Abstract***Introduction*

Patients with cancer in esophagus and gastroesophageal junction (EGEJ) treated with chemoradiotherapy (chemoRT) have increased risk of cardiovascular disease. EGEJ patients often have frailty and pre-existing cardiovascular disease. This may disqualify them for standard trimodal curative treatment and offer surgery alone, chemoRT alone or palliative treatment only. The current understanding of radiation induced heart disease (RIHD) in EGEJ patients is limited. Hence, there is a need for additional studies. Especially on myocardial function during and after chemoRT as congestive heart failure is a serious complication associated with increased morbidity and mortality. Proton-based radiation therapy (RT) is a new alternative to standard photon-based radiation therapy, that is likely to reduce the risk of cardiovascular complications.

*Hypothesis*

Treatment with chemoRT might induce myocardial dysfunction, symptoms of heart failure and decreased physical performance in patients with EGEJ Cancer.

*The aim*

Is to investigate the influence on chemoRT on myocardial function in EGEJ patients and evaluate the cardiac prognosis and eventually identify potential high-risk patients who might benefit from proton-based RT instead of the current photon-based RT.

*Method*

From power calculation we plan to include 56 patients with EGEJ cancer during a period of two years. Inclusions criteria: biopsy verified EGEJ cancer supported by findings from gastroscopy, PET CT scan and with the final diagnosis locally advanced, non-metastatic. The patients will be examined with serial cardiac investigations to evaluate if they develop impairment of the heart function during or after chemoRT. The investigations include; electrocardiogram, cardiac biomarkers, echocardiography and cardio pulmonary exercise test. The examinations will be performed at study entry (baseline), after two, four, and six weeks and again after six months.

*Status*

The study is planned to start May 2018.

**Clinical trials + Organisation of treatment****Abstract title****#24 Consequences of introducing geometric GTV to CTV margin expansion in DAHANCA contouring guidelines for head and neck radiotherapy****Presenting author**

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**Abstract***Background and purpose*

Defining margins around the Gross Tumour Volume (GTV) to create a Clinical Target Volume (CTV) for head and neck cancer radiotherapy has traditionally been based on presumed knowledge of anatomical routes of spread. However, using a concentric geometric expansion around the GTV may be more reproducible. The purpose of this study was to analyse the inter-observer consistency of geometric CTV delineation with adaptation for anatomical boundaries versus anatomically defined CTVs.

*Material and methods*

Radiation oncologists at four Danish cancer centres delineated high, intermediate and elective dose CTVs (CTV1, CTV2 and CTV3, respectively) in a patient-case template (stage IV squamous cell carcinoma of the oropharynx), first using mainly anatomical margins (original standard) and then using concentric geometric expansion (new standard). Each centre made a dummy-run radiotherapy plan based on the delineated CTVs. The difference between the CTV contours and the radiotherapy plans was evaluated across the centres.

*Results*

Anatomy-based contours were significantly more heterogenous and showed larger volume differences between centres than geometric margins. Dice similarity coefficient increased by 0.29 and mean surface distance decreased by 4 mm for CTV1. Use of consistent CTV volumes resulted in more consistent irradiated volumes between centres.

*Conclusion*

Introduction of geometric margins resulted in more uniform CTV1 and CTV2 delineation. Geometric CTV expansion was easier, left less room for misinterpretation, and resulted in more uniform treatment plans with similar irradiated high and intermediate dose volumes across all centres.

**Clinical trials + Organisation of treatment****Abstract title****#25 Targeted ultrasound and fine needle aspiration cytology for sentinel node diagnostics in early-stage melanoma – a validation study****Presenting author**

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**Abstract***Introduction*

Ultrasound guided fine needle aspiration cytology (US-FNAC) is used to evaluate the involvement of lymph nodes in various malignant diseases. Its value in detecting sentinel lymph node metastasis preoperatively in melanoma patients is controversial and is the subject of this study.

*Material and Methods*

In this prospective validation study, 91 consecutive patients with melanoma clinical stage I (n=64) and II (n=27) were examined with US-FNAC prior to sentinel node biopsy, from 2012 to 2014 at a tertiary center. All patients underwent lymphoscintigraphy prior to the US-FNAC. Lymph nodes that exhibited any of the Berlin morphologic criteria on ultrasonography were examined using FNAC.

*Results*

Median Breslow thickness of the melanomas were 1.22 mm (range 0.47-11.5). Twenty-two percent of the patients had metastases in their sentinel nodes, 90 % of which were smaller than 2mm in largest diameter. The percentages of metastases with a size >1mm were 50 % and 29 %, respectively, in the true positive and false negative US-groups. Sensitivity, specificity, positive predictive value, negative predictive value for overall US examination were 30 %, 81 %, 24 %, 83 %. None of the FNACs contained conclusive malignant cells. The specificity of the FNAC was 76 %.

*Conclusions*

Our results show that US-FNAC was not a helpful diagnostic tool in our setting, as it did not add significantly to the staging and management of patients with mainly thin cutaneous melanomas, perhaps due to the often small size of the SN metastases. It may be useful in early diagnosis of lymph node metastases in a subgroup of melanoma patients with larger metastases.



**Clinical trials + Organisation of treatment****Abstract title****#26 Evaluation of groin lymphadenectomy extent for metastatic melanoma (The EAGLE FM Study) - inguinal or ilio-inguinal lymphadenectomy for patients with metastatic melanoma to groin lymph nodes and no evidence of pelvic disease on PET/CT Scan – a randomised phase III trial****Presenting author**

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**Abstract***Background and Rationale*

Spread of metastatic melanoma to the groin lymph nodes (LN) is a common event for patients with melanoma. In melanoma treatment centres around the world, patients without demonstrated pelvic LN disease receive 1 of 3 strategies of management in relatively equal proportions:

- i. Inguinal Lymphadenectomy (IL)
- ii. Ilio-inguinal Lymphadenectomy (I-IL)
- iii. Variable use of either IL or I-IL surgery.

Some larger melanoma centres have an institutional policy that all patients have either IL or I-IL for metastatic inguinal node involvement. Nearly all centres would agree that patients with pelvic LN involvement without distant metastatic disease should have I-IL.

*Study Objectives*

This study aims to provide a more rational evidence base for appropriate management for metastatic melanoma in the groin LNs, through assessing the effect of the addition of ipsilateral pelvic lymphadenectomy on patient disease-free survival (DFS), distant disease-free survival (DDFS), overall survival (OS), morbidity, and quality of life. In addition, the study will clarify the reliability of PET (Positron Emission Tomography) / CT (Computed Tomography) scans for staging pelvic LNs, clarify morbidity differences between the operations in a balanced cohort, evaluate any health economic benefits of I-IL over IL and provide a tissue and serum resource to be used to identify biological markers of recurrence and progression after inguinal metastases.

*Study Hypothesis*

There will be no significant difference in DFS between patients having IL or I-IL, conditional on PET/CT scan showing no evidence of pelvic disease at the time of diagnosis of groin LN metastatic melanoma.

*Study Population*

The aim is to recruit 634 patients in 5 years with cytologically or histologically confirmed metastatic melanoma in inguinal LNs; specifically with no evidence of pelvic node involvement or distant spread of melanoma clinically or on PET/CT staging scans.

*Study Treatments*

Eligible patients will be randomised 1:1 to undergo an IL or I-IL.

*Study Design*

This is an international, multi-centre, phase III, non-inferiority, prospective, randomised clinical trial. In Denmark it is planned to run at Dep of Plastic Surgery, Herlev Hospital, and Clinic of Plastic Surgery, Breast Surgery and Burns, Rigshospitalet.

**Clinical trials + Organisation of treatment****Abstract title****#27 Værdien af cirkulerende tumor DNA for tidlig opsporing af tilbagefald af modernærkekræft****Presenting author**

Annette Chakera

**Authors and affiliation**

Annette Chakera og Lisbet Hølmich, Herlev Hospital; Grethe Schmidt, Rigshospitalet; Lars Stolle, Aarhus Universitetshospital; Robyn Saw, Melanoma Institute Australia

**Abstract**

Formålet med dette pilot-studie er at undersøge, om man tidligt kan diagnosticere tilbagefald af modernærkekræft hos patienter i høj risiko for tilbagefald, ved at måle DNA fra kræften (cirkulerende tumor DNA, ctDNA) i en simpel blodprøve ved hvert kontrolbesøg.

I øjeblikket kontrolleres modernærkekræft-patienter i Danmark i høj risiko for tilbagefald med klinisk undersøgelse hver 3. måned i 2 år og derefter hver 6. måned til ialt 5 år, og helkrops-PET-CT scanninger efter 6, 12, 24 og 36 måneder. Ulempen ved PET-CT scanninger er, at de kun kan finde metastaser af en vis størrelse, giver en høj stråledosis og er dyre. Den eneste rutinemæssigt accepterede biomarkør for modernærkekræft er LDH, men den er hverken følsom eller specifik nok til at diagnosticere tilbagefald tidligt. ctDNA har vist sig at være lovende som biomarkør til at kontrollere respons på kræftbehandling hos patienter som allerede har spredning af modernærkekræft. Denne simple blodprøve, som kan gentages og er relativt billig, kan muligvis også bruges til at opdage tilbagefald hos patienter i kontrolforløb – men det er endnu ikke undersøgt. Hypotesen er, at ctDNA kan diagnosticere tilbagefald samtidig med, eller måske tidligere, end det kan ses på PET-CT scanninger. Er det tilfældet kan metoden muligvis ændre behandlingen, forbedre prognosen og mindske brug af PET-CT scanninger. ctDNA på diagnostetidspunktet kan muligvis også bruges til at diagnosticere patienter, som har særlig høj risiko for tilbagefald og som kan have gavn af ekstra tæt kontrol.

Studiet er et "proof-of-concept" studie, som baserer sig på analyse af ctDNA i blodprøver og sammenligning med LDH (og vitamin-D og CRP) og PET-CT scanninger og typen af modernærkekræft. Studiet er designet til at indsamle blodprøver ved hvert kontrolbesøg hos patienter i høj risiko for tilbagefald af modernærkekræft, d.v.s. ved inklusion i forsøget, hver 3. måned i 2 år og derefter hver 6. måned i yderligere 3 år. Der forventes at blive inkluderet ca. 300 deltagere i forsøget; fra Danmark forventes deltagelse af ca. 160-180 patienter fra Plastikkirurgisk Afdeling, Herlev Hospital, på Plastikkirurgisk Afdeling, Aarhus Universitetshospital, på Klinik for Plastikkirurgi, Rigshospitalet, og fra Melanoma Institute Australia, Sydney, Australien.

**Clinical trials + Organisation of treatment****Abstract title****#28 Efficacy of immunotherapy in melanoma patients with brain metastases treated with steroids – the MEMBRAINS trial****Presenting author**

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**Abstract***Introduction*

Steroids are the mainstay of symptomatic treatment for brain metastases. Over 15% of patients diagnosed with metastatic melanoma receive treatment with steroids already at first oncological evaluation. However, this sizable group of patients is not represented in any prospective clinical trial of cancer immunotherapy. The purpose of this clinical trial is to clarify whether treatment with a CPI alone or two in combination, results in clinical benefit for MM patients with brain metastases and in need of steroid treatment. In addition a translational program is established in the search for predictive or prognostic factors.

*Materials and methods*

The clinical trial is designed as an open-label non-randomized phase II trial with four arms depending on steroid dose level (>10-25 mg or >25 mg) and treatment with either pembrolizumab alone or ipilimumab in combination with nivolumab. In the pilot phase six patients will be enrolled in each arm, and if at least one patient has clinical benefit defined as complete response, partial response or stable disease  $\geq$  6 months, individual arms will be expanded to enroll a total of 20 patients. Primary endpoints are progression-free survival and overall survival rates at 6 months. Patients are evaluated clinically and with regular PET/CT scans and MRI of the brain. For translational purposes blood samples are drawn before treatment and at multiple time points following treatment initiation.

**Clinical trials + Organisation of treatment****Abstract title****#29 T-cell therapy in combination with vemurafenib in BRAF mutated metastatic melanoma patients****Presenting author**

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**Abstract***Introduction*

Despite impressive response rates following adoptive transfer of autologous tumor infiltrating lymphocytes (TILs) in metastatic melanoma, improvements of therapy are needed. In this clinical trial, we evaluated the combination of TILs and pretreatment with vemurafenib, a small-molecule BRAF inhibitor with immunomodulatory properties (ClinicalTrials.gov ID NCT02354690).

*Materials and methods*

In this open phase II clinical trial patients were pretreated with vemurafenib for seven days prior to tumor excision and the following weeks during T-cell manufacturing. TILs were grown from tumor fragments in vitro and re-infused into the patient preceded by a lymphodepleting chemotherapy regimen and followed by interleukin-2 infusion. Vemurafenib was discontinued 7 days before TIL infusion.

Primary endpoint was to evaluate feasibility and safety. Secondary endpoint was to evaluate clinical response rate according to RECIST 1.1.

*Results*

A total of 13 patients were included following progression after anti-PD-1 and/or anti-CTLA-4 treatment. No unexpected toxicity was observed and treatment was well tolerated. Clinical response evaluation to combined treatment is still ongoing and so far one patient achieved complete response (ongoing), eight patients achieved confirmed partial response (seven confirmed of which one is ongoing), two achieved stable disease, one is not yet evaluated, and one was excluded before treatment with TILs as it was deemed unsafe to treat with TIL therapy due to an uncontrolled brain metastasis.

*Conclusions*

Pretreatment with vemurafenib before infusion of TILs was safe and feasible and induced objective clinical responses in this difficult-to-treat cohort of patients with melanoma resistant to anti-PD-1 and/or anti-CTLA-4.

**Clinical trials + Organisation of treatment****Abstract title****#30 TIL-based adoptive cell therapy across all cancer diagnoses in combination with checkpoint inhibition****Presenting author**

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**Abstract***Background*

Immune therapy based on adoptive cell therapy (ACT) with ex vivo expanded tumor-infiltrating lymphocytes (TILs) has been tested in late stage malignant melanoma (MM) with impressive response rates. The very presence of TILs indicates immune reactivity and is in itself a prognostic marker for the clinical outcome of many malignancies including MM. Meanwhile, the indication for immune therapy with checkpoint inhibitors is constantly expanded to new cancer diagnoses. We wish to test the safety, feasibility and therapeutic potential of TIL-based ACT across all cancer diagnoses.

*Methods*

25 patients with different metastatic cancers will be recruited and treated with TIL-based ACT at Herlev Hospital during the next 2 years. From each patient a tumor is surgically resected and a TIL product is produced. Prior to the TIL infusion the patients are hospitalized and undergo lymphodepletive chemotherapy. TIL infusion is followed by 2 weeks of immune stimulatory treatment with low dose subcutaneous IL-2 injections. The therapy is combined with one dose of ipilimumab before surgery and four doses of nivolumab after TIL infusion. The primary endpoint is safety and feasibility. The patients will be evaluated with radiologic clinical responses according to RECIST 1.1.

*Results*

The clinical trial is ongoing and the results are preliminary. In 8 out of 10 patients a viable TIL product has successfully been expanded ex vivo. So far, 6 patients (2 ocular melanoma, 2 head-and-neck and 2 colon cancer) have received their expanded TIL product in combination with checkpoint inhibition and the toxicity has been acceptable.

*Conclusion*

TIL-based ACT appears to be safe and feasible in malignancies outside of MM. At the end of this study, we will be able to report clinical response rates to TIL-based ACT in several different and untested malignancies.

**Clinical trials + Organisation of treatment****Abstract title****#31 Beating cancer cachexia: a multimodal, cachexia-preventing intervention in patients with inoperable, non-small cell lung cancer (LUCANU-2)****Presenting author**

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**Authors**

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**Abstract***Introduction*

Cancer cachexia is associated with impaired physical function, reduced tolerance to anticancer treatments and reduced survival of patients with non-small cell lung cancer (NSCLC). Early intervention is crucial to prevent severe cachexia. International guidelines suggest multimodal intervention, targeting the three aspects of cachexia: loss of muscle mass, decreased dietary intake, and inflammation.

*Method*

In the current study feasibility intervention study 70 patients with inoperable NSCLC will, during the first 9-12 weeks of systemic anti-neoplastic treatment (chemotherapy or immune-checkpoint inhibitor), receive a physical training program, nutritional counselling, and fish oil. Physical training consist of two exercises: sit-to-stand strength exercise and brisk walking. The aim of the nutritional intervention is to reach an energy intake of 30 kcal/kg/d, at least 1.0g protein/kg/d, three daily meals of a minimum of 20g protein and maximum 11 hours overnight fasting. Patients receive dietetic counselling on a regular basis and nutritional support when necessary. Finally, patients receive 2 g eicosanoids + docosahexaenoids daily, either as liquid or capsules. Body weight, dietary intake and physical function is assessed at every treatment day (4 in total). Muscle mass is estimated by CT-scans at the 3rd lumbar vertebra level (FatViking software) at baseline and after 3 cycles of treatment.

*Results*

Primary outcome is to assess feasibility of the study protocol: accrual rate, attrition rate and adherence to protocol. Secondly, body weight changes, muscle mass and physical function will be assessed and compared to data from the observational study LUCANU-1.

*Conclusion*

In this multimodal interventional study, we will explore the feasibility of an intensive cachexia-prevention programme with the aim of conducting a larger, randomized trial in the future.

**Clinical trials + Organisation of treatment****Abstract title****#32 Impact of comprehensive geriatric assessment on quality of life, overall survival, and unplanned admission in patients with non-small cell lung cancer treated with stereotactic body radiotherapy - results of a randomized study****Presenting author**

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**Abstract***Introduction*

Overall survival (OS) for patients with localized non-small cell lung cancer (NSCLC) treated with stereotactic body radiotherapy (SBRT) is poorer than for patients undergoing surgery. A possible explanation is contribution of comorbidities to the mortality. A comprehensive geriatric assessment (CGA) has been found to improve OS and quality of life (QoL) in older people with non-malignant diseases. This randomized study investigates if a CGA added to SBRT for patients with localized NSCLC impact QoL, survival, and unplanned admission.

*Materials and Methods*

From January 2015 to June 2016, 51 patients diagnosed T1-2N0M0 NSCLC treated with SBRT were enrolled. The patients were randomized 1:1 to receive SBRT ±CGA. EQ-5D QoL health index and VAS scores were assessed at start of SBRT, at five weeks, and every third month for a year after SBRT. Repeated measures ANOVA compared EQ-5D overall scores and changes from baseline. OS was analyzed by Kaplan-Meier methods and compared with log-rank test. The prevalence of unplanned admissions was compared using the  $\chi^2$ -test.

*Results*

There were 26 and 25 patients randomized to receive ±CGA, respectively. The repeated measures ANOVA test of the EQ-5D health index and VAS scores did not show statistically significant differences between groups. For the EQ-5D VAS scores at 12 months follow-up there might be a small difference between the groups although not statistically significant. The 1-year and 2-year OS was 92% vs. 72% and 69% vs. 59% for the groups ±CGA, respectively ( $p=0.32$ ). There was no statistically significant difference in unplanned admissions 46% vs. 52% ( $p=0.68$ ).

*Conclusion*

In patients with localized NSCLC treated with SBRT a CGA did not impact the overall QoL, the prevalence or length of unplanned admissions, or survival. There was an indication of small differences in QoL and survival in the data, but such differences can only be validated in larger studies.

**Clinical trials + Organisation of treatment****Abstract title**

**#33 Sikkerheds- og effektstudie af standard (st.) dosering af Carboplatin dag 1 hver 3. uge plus daglig Navelbine® 20/30 mg (oral) i løbet af 4 cykler (12 uger) til behandling af fremskreden ikke små-cellet lungekræft; et pilot studie**

**Presenting author**

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**Abstract***Rationale*

Uhelbredelig lungekræft er en alvorlig sygdom hvor hovedparten af patienterne desværre dør mellem 10 og 14 måneder efter diagnosen selv hvis de behandles med kemoterapi. Målet for behandling af patienter med metastatisk ikke-små-celle lungekræft (NSCLC) er at lindre symptomerne og forlænge overlevelsen og samtidig give patienten bedst mulige livskvalitet. Derfor skal lindrende behandling afvejes mod overlevelse og toksicitet.

Metronomiske regimer, hvor små, hyppige doser kemoterapi administreres, er blevet foreslået til lavere behandlingsrelaterede toksicitet samtidig med at opretholde eller endog forbedre effekten. De hyppige administrationer har til formål at eksponere kræftceller kontinuerligt for lægemidlet, forebygge kræftcellernes reparation og eventuelt forbedre tumor kontrol.

*Primært mål*

At undersøge bivirknings profillen og tolerabiliteten (grad 2-5 CTC), når Navelbine gives som en lille daglig dosis (metronomisk) sammen med Carboplatin AUC 5 hver 3. uge.

*Metode*

Projektet vil inkludere 20 patienter med uhelbredelig lungekræft, som er kandidat til 1. linie standard kemoterapi. Inklusionen starter fra 1.april 2018 på kræftafdelingen AUH.

Studiet er en åben en-armet-undersøgelse, hvor patienterne bliver tilbudt standard kemoterapi i form af Carboplatin AUC 5 dag 1 (iv. hver 3. uge) og metronomisk kemoterapi i form af kapsel Navelbine® med små doser kemokapsler (20/30 mg) dagligt i 12 uger efterfulgt af en evaluering af behandlingen i henhold til den afdelingens standarder. Under 1. cyklus gives 20 mg Navelbine dagligt, hvis denne dosis tolereres uden grad 3-4 toksicitet, øges dosis til 30 mg dagligt i resten af behandlings periode. Patienterne registrer deres bivirkninger via ambuflex® hver 3. uge i 12 uger.

*Konklusion*

Vi håber at forsøget kan være med til at nedbringe bivirkningerne af vores standard kemoterapi og måske endda øge effekten, da patientgruppen i den grad har et udekket behov for en skånsom men også en effektiv behandling.



**Clinical trials + Organisation of treatment****Abstract title****#34 Tumor-reactive T cell subsets in the microenvironment of ovarian cancer****Presenting author**

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**Abstract***Background*

Solid malignancies are frequently infiltrated with T cells. The success of adoptive cell transfer (ACT) with expanded tumor-infiltrating lymphocytes (TILs) in melanoma warrant its testing in other cancer types. In this preclinical study, we investigated whether clinical-grade TILs could be manufactured from ovarian cancer (OC) tumor specimens.

*Methods*

34 tumor specimens were obtained from 33 individual patients with OC. TILs were analyzed for phenotype, antigen specificity and functionality.

*Results*

Minimally expanded TILs (Young TILs) were successfully established from all patients. Young TILs contained a high frequency of CD3+ cells with a variable CD4/CD8 ratio. TILs could be expanded to clinical numbers. Importantly, recognition of autologous tumor cells was demonstrated in TILs in >50% of the patients. We confirmed with mass-spectrometry the presentation of multiple tumor antigens, including peptides derived from the cancer-testis antigen GAGE, which could be recognized by antigen specific TILs. Antigen specific TILs could be isolated and further expanded in vitro.

*Conclusion*

These findings support the hypothesis that patients with OC can benefit from ACT with TILs, and led to initiation of a pilot clinical trial at our institution (clinicaltrials.gov: NCT02482090).

**Clinical trials + Organisation of treatment****Abstract title****#35 Sentinel node mapping with robotic assisted near infra-red fluorescent imaging in women with endometrial cancer (SENTIREC)****Presenting author**

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**Abstract***Background*

Sentinel node (SN) mapping has proved safe in early stage low-risk endometrial cancer. However, the SN mapping technique has not been widely implemented for this patient group in Denmark and the effect on chronic complications and quality of life has yet to be evaluated.

The aim of the present study is to safely implement this more conservative surgical approach to patients with early stage endometrial cancer. The objectives are to evaluate:

- I. The effect of SN mapping on the incidence of lymphedema in women with early stage endometrial cancer.
- II. The feasibility of applying the SN mapping technique in combination with F-18-FDG-PET/CT imaging in women with high-risk histology endometrial cancer.

*Materials and methods*

- I. Patients with early stage low-risk endometrial cancer are eligible for an observational study where SN mapping is performed instead of radical pelvic lymphadenectomy. The effect on the incidence of lymphedema and quality of life will be assessed using patient reported outcome measures before then prospectively up to 3 years following surgery.
  - II. Patients with high-risk endometrial cancer are eligible for an observational study using SN mapping combined with F-18-FDG-PET/CT imaging to assess their combined accuracy in lymph node metastases assessment.
- Prior to these studies a pilot study of 30 patients at each participating centre must be performed.

*Results*

Four gynaecologic oncology centres in Denmark are participating in this project. Two centres have completed the pilot study where a total of 70 patients were included, showing an overall SN detection rate of 94.3%, hereof 74.2% bilaterally. In Study I, 15 of 100 patients with FIGO IB endometrial cancer have been included. In Study II, 32 of 200 patients with high-risk endometrial cancer have been included.

*Conclusion*

This project may have substantial significance in changing the national treatment strategy of endometrial cancer patients.

**Clinical trials + Organisation of treatment****Abstract title****#36 Improving cervical cancer prevention by introducing HPV self-sampling in the Danish screening program - a randomized controlled trial****Presenting author**

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**Authors**

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**Abstract***Introduction*

Even in countries with organized screening programs, cervical cancer is a burden, especially in un-screened women. This trial, the first of its kind, evaluates if offering HPV self-sampling kits, either mailed directly to the women or using timely opt-in procedures for ordering the kit, increases screening participation when compared with a standard second reminder.

*Methods*

In this randomized controlled trial, 9,791 Danish women aged 30-64 who were due to receive the second reminder were randomized to 1) direct mailing of a second reminder and a self-sampling kit (directly mailed group); 2) mailing a second reminder to order the kit by email, text message, phone, or website (opt-in group); or 3) mailing a second reminder to attend regular cytology screening (control group). Participation was measured at 180 days post intervention, by returning a self-sample or attending regular cytology screening. The proportion of HPV-positive self-samplers who attended follow-up within 90 days was estimated.

*Results*

Participation was significantly higher in the directly mailed group (38.0%) and in the opt-in group (30.9%) than in the control group (25.2%) (differences: 12.8%, 95% CI: 10.6-15.0% and 5.7, 95% CI: 3.5-7.9%, respectively). The directly mailed strategy (19.9%) made significantly more un-screened women participate in screening than the standard procedure (7.2%) (difference: 12.6%, 95% CI: 8.8-16.4%). Of 118 HPV positive self-samplers, 90.7%, 95% CI: 83.9-95.3% attended follow-up.

*Conclusions*

Offering HPV self-sampling as an alternative to regular cytology screening increased participation; the direct mailing strategy was the most effective invitation strategy. High compliance with follow-up occurred. Implementing HPV self-sampling in the Danish screening program may increase screening participation and help recruit un-screened women, thereby improve cervical cancer prevention.

**Clinical trials + Organisation of treatment****Abstract title****#37 Methylphenidate for fatigue in haematological cancer. A randomized, double-blind, placebo-controlled, crossover trial - the MICRO trial****Presenting author**

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**Abstract***Introduction*

Despite improvements in cancer treatment and supportive care in haematological malignancies one of the most prevalent and debilitating symptoms - cancer related fatigue (CRF) - has not improved. Half of patients who have received chemotherapy within the last year report fatigue disproportionate with daily activities that reduces quality of life (QoL), functional capacity, impacts health behavior and recovery. Moreover the single most prevalent and severe unmet need in these patients is "dealing with feeling tired" and no approved treatment exist.

Studies in solid cancer, however, suggest that methylphenidate (MTP) may improve CRF. We aim to study the effects of and safety of MTP treatment on fatigue in haematological cancer patients. A panel of patient representatives evaluated the relevance of the study as high.

*Material and methods*

The trial is a randomized, double-blind, placebo-controlled crossover study including severely fatigued haematological cancer patients from 7 Danish departments. Participants are randomized to 6 weeks of MTP or placebo treatment followed by a 1-week "wash-out" before subsequently crossing over to 6 weeks placebo or MTP treatment. End-points are patient-reported fatigue and QoL, as well as assessments of physical capacity (self-reported and objective evaluations). Fatigue will be assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale and Visual Analogue Scale (VAS) score whereas QoL is evaluated by the EORTC-QLQ-C15-PAL. Toxicity is assessed subjectively (patient-reported) as well as objectively (investigators) using common terminology criteria for adverse events. The study is powered to show a 4.25 point improvement in the FACIT-F score reflecting clinically relevant difference in FACIT-F, and it will include 150 patients.

*Results and conclusions*

This is the first controlled study aiming at improving fatigue in haematological cancer patients. Inclusion starts in May 2018.

**Clinical trials + Organisation of treatment****Abstract title****#38 Prospective, feasibility study of the use of sodium fluorescein in glioma surgery****Presenting author**

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**Authors**

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**Abstract***Introduction*

Glioblastoma (GBM) continues to be the cancer with most years of life lost. Current treatment is maximal extent of resection (EOR) followed by chemotherapy and radiation.

Sodium fluorescein (SF) is a dye in use since 1996 in neurosurgery. With the introduction of the specific YELLOW 560 filter it is now possible to use low dose SF.

SF is comparable to contrast-enhanced tissue due to blood-brain barrier breakdown.

SF has not been used in neurosurgery in Denmark before. This descriptive study aimed to increase EOR in GBM, secondary outcome was feasibility of the method.

*Material and methods*

Prospective, non-randomized study. Patients suspected of GBM were included. 200mg SF was administered intravenously and the surgery was performed using YELLOW 560 filter.

Neuro radiologists compared pre- and postoperative scans. Total resection (TR) was defined as no CE-tissue (contrast enhanced) on the postoperative MRI, near total resection (NTR) defined as non-measurable visible tumor and lastly measurable resection, sub-total resection (STR).

Three neurosurgeons graded SFs ability to locate and remove tumor from 1 (being not helpful) to 4 (being very helpful). Biopsies were taken in fluorescent, non-fluorescent and marginal zone tissue to compare tumor cell aggregation.

*Results*

18 patients were included. 3/18 with TR, 9/18 with NTR and 6/18 with STR. Pooling TR and NTR (as GTR) together gives a total resection rate of 66.7%. Nationwide GTR resection rate was 38% although this includes biopsies.

Biopsies showed a correlation between fluorescent tissue and tumor cell aggregation, 12 patients were graded in terms of SFs ability to locate and remove tumor tissue. Mean for localization is 3.8 and for removal 3.75.

No serious adverse events were registered in patients.

*Conclusions*

This study indicates that the use of SF in GBM resection improved the EOR without serious adverse events. A randomized trial is underway to further document the method.

**Clinical trials + Organisation of treatment****Abstract title****#39 Arginase-1 peptide vaccine in patients with metastatic solid tumors. Clinical trial in progress****Presenting author**

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**Authors**

Svane, I.M. (1,2); Andersen, M.H. (1)

**Abstract***Introduction*

Arginase-1 (ARG1) is a cytoplasmic enzyme that catalyzes the final step of the urea cycle in which arginine is converted to urea. The enzyme is mainly expressed in hepatocytes, but some cancer cells and different myeloid cells are also capable of high ARG1-expression. ARG1-induced arginine depletion suppresses T cell function through the impairment of the T cell receptor (TCR)-complex. National Center for Cancer Immune Therapy (CCIT-DK) has identified spontaneous T cell reactivity against ARG1 peptides in peripheral blood mononuclear cells of cancer patients and healthy donors. The theoretic background for a peptide vaccine against ARG1 is to boost the activity of ARG1-specific T cells to engage and eliminate ARG1-expressing cells in the local immunosuppressive microenvironment in cancerous tissues.

*Materials and methods*

In this clinical phase I study we aim to treat 10 patients with progressive, persistent, or recurrent solid tumors following treatment with standard of care agents. Patients will receive ARG1 vaccinations administered subcutaneously every third week for 46 weeks. The primary endpoint is to evaluate toxicity according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Anti-tumor immune responses will be assessed using blood and tumor tissue samples and objective responses are evaluated using RECIST 1.1.

*Conclusion*

The enzyme ARG1 inhibits T cell function by reducing the availability of arginine to T cells in the tumor microenvironment. In this phase I study we are planning to treat 10 cancer patients with an ARG1-peptide vaccine. The aim is to boost ARG1-specific T cells to ameliorate the elimination ARG1-expressing cells in the local immunosuppressive tumor environment.

**Clinical trials + Organisation of treatment****Abstract title****#40 Morbidity after cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) used in treatment of ovarian, tubal and primary peritoneal cancer****Presenting author**

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**Abstract***Introduction*

Cytoreductive surgery (CRS) is increasingly used in treatment of ovarian, tubal and primary peritoneal cancer (OC). Hyperthermic intraperitoneal chemotherapy (HIPEC) consists of intra-operative perfusion of the abdominal cavity with a heated solution with a cytotoxic agent aiming to prevent disease recurrence. Study aims were to evaluate morbidity and mortality of CRS combined with HIPEC in OC patients.

*Methods*

In a pilot study 25 patients were treated with CRS+HIPEC using carboplatin 800 mg/m<sup>2</sup> for 90 minutes. Inclusion criteria: Patients with primary OC FIGO stages III-IV subjected to up-front or interval CRS, age 18-75 years, American Society of Anaesthesiologists (ASA) scores I-II and complete cytoreduction (i.e. no visible tumour nodules in the abdominal cavity after the surgical procedure). For stage IV, only patients with resectable disease and patients with complete remission of extra-abdominal metastasis after neoadjuvant chemotherapy. Study endpoints: 30-day mortality and adverse events as assessed by Common Terminology Criteria for Adverse Events (CTCAE). Severe and life-threatening (grade III/IV) complications are reported.

*Results*

Median (range) age was 58 (39-73) years. Fourteen patients had up-front CRS and 11 patients had interval CRS. Median Peritoneal Cancer Index was 11 (5-32). No deaths occurred within 30 days. Reoperation was necessary in two patients (8.0%): a stoma revision 27 days post-surgery and intraabdominal hemorrhage after removal of drainage tube three days post-surgery. Eleven patients experienced at least one grade III complication (44.0%), and the most frequent was fever/infection with unknown origin (n=3, 12.0%), transient neutropenia (n=3, 12.0%) and peritonitis/intraabdominal abscess (n=3, 12.0%). There were no grade IV complications.

*Conclusion*

CRS+HIPEC with carboplatin 800mg/m<sup>2</sup> used for selected patients with advanced stage OC is feasible with an acceptable morbidity in present pilot study.

**Clinical trials + Organisation of treatment****Abstract title****#41 PIPAC (Pressurized IntraPeritoneal Aerosol Chemotherapy) in the prevention and treatment of peritoneal metastasis****Presenting author**

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**Abstract***Introduction*

Peritoneal metastasis (PM) represents end stage disease in many types of cancer and systemic chemotherapy has limited effect on PM. Curative treatment of manifest PM is only possible in a highly selected fraction of patients, and the majority of patients with PM will die within six months from diagnosis. Realizing these limitations in PM treatment, the ideal concept would be to identify high risk cancer patients and treat them prophylactically, and to develop an effective treatment of manifest PM

*Methods*

PIPAC is a new technique where aerosolized chemotherapy is emitted directly inside the abdominal cavity during laparoscopy. PIPAC ensures a high concentration of chemotherapy in the PM without the side effects of systemic chemotherapy. Treatment response is monitored through repeated evaluation of biopsies and peritoneal fluid collections. The first Scandinavian PIPAC procedure was performed at Odense University Hospital in 2015.

*Results*

Since 2015, Odense PIPAC Center has performed more than 200 protocolled PIPAC procedures in 69 patients with PM from different diseases. No occupational health risk or severe complications were seen and the majority of patients were discharged within 24 hours. 72% (50/69) of the patients had  $\geq 2$  PIPAC treatments, and objective treatment response was seen in 54% (27/50). PIPAC was able to stabilize and maintain the patients' quality-of-life during treatment. A new multi-center study has been initiated, where PIPAC is used to prevent the development of PM in high-risk patients operated for colon cancer, and a similar study is being prepared for gastric cancer patients.

*Conclusion*

PIPAC shows significant treatment response in patients with manifest PM, and PIPAC has the potential to prevent the development of PM in high-risk patients. Odense PIPAC Center is the only center in Scandinavia performing this new minimal invasive, lenient and safe procedure, but patients are referred from both abroad and other Danish regions.



**Clinical trials + Organisation of treatment****Abstract title****#42 An open multicenter study to investigate efficacy and tolerability of olanzapine in patients with advanced cancer suffering from nausea not induced by chemotherapy or irradiation****Presenting author**

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**Abstract***Introduction*

The anti-psychotic drug olanzapine is of interest because it is effective against chemotherapy-induced nausea and targets multiple receptors known to be involved in the emetic reflex arch. The drug has a half-life of 30 hours, which allows for a single daily administration.

*Objectives*

To investigate the anti-emetic effect and tolerability of olanzapine in patients with advanced cancer not receiving chemotherapy or irradiation.

*Methods*

Patients with advanced cancer (no curable treatment options) with at least 'moderate' nausea and/or one emetic episode within 24 hours were included if they had not received chemotherapy or irradiation within the previous 14 days and had no reversible causes of nausea/vomiting. The patients were administered 10 mg olanzapine daily for five days (first dose subcutaneously and the following four orally). Nausea, vomiting and adverse effects were assessed for seven days.

*Results*

Twenty-one patients have been included. Eighteen patients experienced some degree of improvement. Mean combined N/V score (0-100) at baseline was 68. After 24 hours and seven days it was 20 and 21, respectively. We recorded no extrapyramidal symptoms, hypotension or seizures. Fatigue, dizziness and sedation were numerically (but not statistically significant) worse 24 hours after the first dose. No adverse events seemed to be present at seven days.

*Conclusions*

Olanzapine appears effective and tolerable as an anti-emetic in patients with advanced cancer. Recruitment continues and updated results will be presented.

Future research should examine a lower dose (5 or 2.5 mg), preferably in a randomized controlled trial.

**Clinical trials + Organisation of treatment****Abstract title****#43 Effects of topical zinc on epidermal wound healing studied by quantitative immunohistochemistry****Presenting author**

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**Authors**

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**Abstract***Introduction*

Zinc sulfate is added to many dermatological formulations but its roles during epidermal regeneration are poorly understood. We have investigated the effect of topical zinc on biomarkers of epidermal wound healing in a randomized double-blind trial.

*Material and methods*

One uniform epidermal wound was made by suction on each buttock of 30 healthy volunteers and randomized to zinc sulfate (1.4%) gel (n = 20), placebo gel (n = 20), or control (n = 20) treatment. On postwounding day 4, biopsies of the wounds including periwound skin were fixed in paraformaldehyde, embedded in paraffin and sections immunostained in the Dako Autostainer with monoclonal antibodies against metallothionein-1 (MT- 1), Ki-67 and matrix metalloproteinase-1 (MMP-1). Slides were scanned and quantitative image analysis performed using the same optimized algorithm for respective antigen. Immunostaining was expressed as percentage of positive cells to the total number of cells.

*Results*

An intact basal lamina of the wounds was confirmed by PAS staining. Increased ( $p < 0.001$ ) epidermal MT and Ki-67 immunostaining was observed in proliferating keratinocytes at the wound edge and migrating epidermal tongue compared with adjacent skin. Increased MMP-1 immunostaining was restricted to the migrating epidermal tongue. Ki-67 epidermal labeling index decreased significantly with zinc treatment. In the dermal compartment, zinc increased MT-1 and MMP-1 expression beneath the neopeidermis and in the wound bed.

*Conclusion*

Quantitative immunohistochemistry proved useful in elucidating the mechanisms of action of zinc. The increased MT-1 expression may account for the anti-inflammatory effects of zinc and the increased MMP-1 for acceleration of keratinocyte migration.

**Clinical trials + Organisation of treatment****Abstract title****#44 National status på implementering af MDT-konferencen - valideringsproces af spørgeskema som grundlag for kvalitativ analyse****Presenting author**

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**Abstract***Introduktion*

MDT-udvalget undersøger status for implementering af MDT-konferencen – herunder identificeres udfordringer og vellykkede initiativer ud fra individuelle oplevelser samt udviklingsområder for MDT-konferencerne. Spørgeskemaet er pilottestet på udvalgets egne MDT-konferencer mhp. validering. I undersøgelsen indgår de fire kræftsygdomme med størst patientvolumen.

*Materiale og metode*

750 MDT-deltagere indenfor mamma-, lunge-, kolorektal- og prostatacancer er inkluderet og har modtaget spørgeskema pr. mail gennem egen MDT-leder. Spørgeskemaer er udsendt til MDT-ledere 24. april, og af disse sendt videre til deres respektive MDT-konferencemedlemmer. Svarfrist er 15. maj efterfulgt af rykkerperiode på 14 dage. Kodning og analyse pågår efterfølgende juni – september.

Udvalget har valgt en kvalitativ tilgang baseret på Most Significant Change-metoden (MSC). Valg af MSC-metoden er begrundet i metodens evne til at indfange stor variation i svar og i kultur samt grad af implementering af alle MDT-konferencens facetter som skitseret i vejledning for MDT-konferencen.

Data analyseres med assistance fra softwaren NVivo. Validitet sikres blandt andet via forskertrianglering, idet kodning foretages inductivt af tre medlemmer af gruppen og valideres af udvalget. Endvidere har de 22 svar fra pilottesten været anvendt til endelig udformning af spørgeskemaet.

*Resultater*

Vi forventer at kunne præsentere præliminære resultater ultimo august. Analysen forventes at give muligheder for at udpege indsatsområder, gående fra simple, nemt implementerbare forslag (fx planlægning og kontrol) til komplekse forslag (fx udvikling af sociale relationer og koordinering af teknisk ekspertise).

*Konklusion*

På basis af de præliminære resultater forventer vi at kunne vise en række tendenser. Vi forventer endvidere at kunne konkludere omkring værdien af kvalitative analysemetoder.

**Clinical trials + Organisation of treatment****Abstract title****#45 The GBM biobank at Biomedicine****Presenting author**

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Pilgaard L. and Duroux M.

**Abstract**

Glioblastoma (GBM) tumors are highly invasive and heterogeneous making them impossible to remove surgically. Even with radical resection, concomitant chemo- and radiotherapy the prognosis is very dismal. Recent studies on the GBM subtypes and interpatient variability renders a move to more personalized treatment strategies. Biobanks are comprehensive collections of biological material correlated to clinical data and they are regarded as an essential resource for discovering new therapeutic targets and customizing treatment. This poster presents a biological resource for the GBM community, a biobank of tissue, cells and blood applicable for GBM research.

The GBM biobank at Biomedicine, Aalborg University is comprised of two biobank sections, each approved by the local ethical committee (N-20100069 and N-20130025). One section was built in collaboration with the Neurosurgery department at Aalborg University Hospital (AAUH) and contains tumor tissue, isolated GBM cells and plasma samples pre-GBM tumor resection. The other section opened in 2013 in collaboration with the Oncology Department, AAUH. To date, it constitutes plasma samples collected post-operatively from 100 glioma patients during the concomitant chemo- and radiotherapy. The database supporting the biobank continues to grow with the addition of clinical data and experimental findings.

The biobank has already resulted in the identification of Cripto-1 as a new biomarker in GBM with a correlation between plasma concentrations and overall survival. This finding has been the foundation for several projects and two current PhD studies. We plan an expansion of the existing biobank and novel protein analysis of the current savings. With further addition of clinical data, the biobank could be the motherboard for answering many future GBM research questions. This we hope will lead to discovery of new biomarkers, potential therapeutic targets and development of prognostic strategies for GBM patients.

**Clinical trials + Organisation of treatment****Abstract title****#46 Integrating basic science, surgery, anesthesiology and oncology for improving short and long-term oncological outcomes: The Enhanced Perioperative Oncology Consortium****Presenting author**

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**Authors**

Gögenur I, Gehl KJ, Troelsen J

**Abstract**

One in three patients will have a recurrence after surgery for colorectal cancer. Factors affecting the immune response in relation to surgery are believed to be central for the recurrence risk.

In a multidisciplinary approach, we created The Enhanced Perioperative Oncology Consortium with support from Zealand University Hospital.

Essential for the consortium is the integration of scientists and clinicians within basic sciences, anesthesiology, epidemiology, surgery, and oncology. The structure of the consortium is multidisciplinary, and the approach for improving perioperative care is multimodal. The Consortium has been divided into seven work packages focusing on the entire course of the patient that is planned for surgical treatment for colorectal cancer. Thus, we have focused on preoperative interventions such as prehabilitation, optimization of immunological function (electrochemotherapy or calcium electroporation pre-operatively, metformin treatment, interferon treatment and modulation of the intestinal microbiome), improved anesthetic and surgical care and finally improved postoperative medical and oncological treatment.

In order to demonstrate the effects of multimodal interventions, we are supplementing the research strategy with in vitro trials and animal research.

The majority of the trials are proof-of-concept randomized controlled trials with use of a translational scientific approach developing markers for measuring the response of our experimental interventions. The goal is to use the results from these trials in future randomized phase III trials with clinical outcomes.

**Clinical trials + Organisation of treatment****Abstract title****#47 Costs and consequences of introducing robotic surgery for women with gynecological cancer****Presenting author**

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**Abstract***Introduction*

The demand for more advanced medical technologies is growing. Robotic Minimally Invasive Surgery (RMIS) is the latest technology and assumed to be more expensive in the short-run compared to Laparoscopic Minimally Invasive Surgery (LMIS) and Open Abdominal Hysterectomy (OAH). RMIS has been rapidly adopted in the treatment of gynecological cancer, and is increasingly used for advanced surgical procedures.

Aim: To evaluate the costs and consequences of RMIS compared to LMIS and OAH in women with endometrial cancer.

*Materials and methods*

A register-based study comprising 5,700 women from the Danish Gynecological Cancer Database. Data are linked in Statistics Denmark with comprehensive information on visits in all hospitals, activities in primary healthcare, prescription medication and social data such as education, labor market affiliation, income, and unemployment benefit reimbursement.

The study consists of:

1. A systematic review evaluating costing methodology for robotic surgery in gynecology.
2. Evaluation of the societal costs of RMIS in the Region of Southern Denmark.
3. Assessment of changes in long-term costs and consequences of RMIS. Nationwide register data will be used for the analysis.

*Results*

The review found that inadequate reporting of the study perspective, short-term horizon, and use of charge data decreased the methodological quality.

Further results will be provided; comparing the costs and consequences before and after the introduction of RMIS with LMIS and OAH.

*Conclusions*

In Denmark there is a unique possibility to follow high quality health care data over time. This project provides comprehensive analysis using the societal perspective with a long follow-up.

**Clinical trials + Organisation of treatment****Abstract title****#48 Odense Pancreas Center (OPAC) – Center of Clinical Excellence: A true multi-disciplinary approach to research in pancreatic cancer and a potential cornerstone in the DCCC supported national strategy****Presenting author**

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**Abstract***Introduction*

Pancreatic cancer (PC) patients have an extremely poor prognosis, and the median overall survival for Danish PC patients is 8 months. Despite this desperate situation, PC treatment and research have gained momentum during the last decade and significant improvements have been made. Although small research units conduct important trials in PC patients, these initiatives are often highly selected, whereas multi-disciplinary approaches covering the translational research gap are rare. The organization and infra-structure of a small nation like Denmark should enable the creation of a national and true multi-disciplinary research structure, but this will necessitate close collaboration between national initiatives and dedicated local research centers.

*Materials, Methods & Results*

After a rigorous application process including peer review by an international expert committee, Odense Pancreas Center (OPAC) was appointed Center of Clinical Excellence by the Region of Southern Denmark in July 2017. OPAC is a multidisciplinary, brick-less research center located at Odense University Hospital, including ten specialties, ten professors, and numerous researchers. An international Advisory Board has been officially appointed to oversee the development and to serve as OPAC advisors. The multi-disciplinary concept of OPAC also includes trials and improvements in basic patient care by specialized nurses and dietitians and physiotherapists – working closely with both patients and their relatives.

The first OPAC results demonstrate the advantages of our multidisciplinary approach, providing mutual inspiration, support and collaboration.

*Conclusion*

OPAC is the first officially supported multi-disciplinary Danish research center focusing on PC. A national and DCCC supported effort should strive to integrate DPCG, its national database (DPCD), and existing centers like OPAC. Such an approach will significantly improve the outcome for Danish PC patients in the future.

**Clinical trials + Organisation of treatment****Abstract title****#49 Uddannelse, professionel og offentlig vidensdeling: En del af strategien for Nationalt Forskningscenter for Stråleterapi****Presenting author**

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**Authors**

Eriksen JG, Laursen LV, Grau C på vegne af Nationalt Forskningscenter for Stråleterapi

**Abstract***Introduktion*

En vigtig del af filosofien bag Nationalt Forskningscenter for Stråleterapi er, at viden skabt i de forskellige projekter formidles bredt. Dette vil ske gennem Ph.D. kurser, workshops og ved at skabe en offentlig bevidsthed om fremskridt ved hjælp af en ny webside, sociale medier og pressen. Ambitionen er at den nye hjemmeside bliver stedet hvor professionelle og offentligheden – patienter, pårørende og pressen – finder information om stråleterapi i Danmark.

*Materiale og metoder*

På baggrund af de ideer diskuteret i arbejdsgruppen samt feedback fra deltagerne (fagfolk, repræsentanter for DCCC og patientrepræsentant) under kick-off-mødet for Forskningscenteret, foreslår vi, at uddannelse og vidensformidling foregår på flere niveauer:

- Ph.D. kurser / workshops, der skal udvikles specifikt til de studerende i forsknings-netværket, helst i samarbejde med Ph.d. skolerne på universiteterne.
  - Møder/symposier hvor forsknings-netværket og DCCC præsenterer og diskuterer resultater og fremskridt internt og med patientrepræsentanter.
  - Online møder for forskningsgrupperne. Vi vil levere projektstyringsværktøjer til deling af dokumenter, hurtig informationsdeling og information online. Derudover vil vi tilbyde et webmødeværktøj med videofaciliteter.
  - Oprettelse af en webside som gør det muligt for offentligheden at blive informeret om projekternes fremskridt.
- Baseret på de aktive diskussioner og input fra fagfolk, DCCC og patientrepræsentant på kick-off-mødet vil vi fokusere på en webside der giver baggrundsinformation om stråleterapi, de nyeste landvindinger, resultater fra projekter i Forskningscenteret, information om åbne protokoller og kontaktmulighed til forskerne.

*Forventede resultater og konklusion*

Ambitionen er at skabe de kurser/workshops, der er relevante for uddannelse inden for Forskningscenteret og at websiden vil være det primære sted for information for patienter, journalister, politikere og andre med interesse i strålebehandling.



**Clinical trials + Organisation of treatment****Abstract title****#50 MR-vejledt strålebehandling af kræftpatienter: Implementering af en MR-accelerator i Region Syddanmark på Odense Universitetshospital****Presenting author**

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**Authors**

Schytte T, Bernchou U, Brink C, Mahmood F, Hansen O, Bertelsen A

**Abstract***Introduktion*

Region Syddanmark har købt en magnetisk resonans accelerator (MR-acc.) til installation på Odense Universitetshospital. Den består af en 1,5 T MR skanner, der kan give MR billeder af diagnostisk kvalitet og af en acc., der kan give strålebehandling (RT). Denne konstruktion giver mulighed for at lave skræddersyet RT tilpasset patientens (pt) anatomi dagligt.

Der er en række fordele ved MR-vejledt RT: I dag laves en simpel CT-scanning før hver RT for at sikre placering af tumor og risikoorgane. CT er dog ikke god til at differentiere mellem forskellige typer blødt væv. For at imødegå dette tillægges en sikkerhedsmargin til det volumen der behandles. På MR billederne er det lettere at se forskel på vævstyperne, og man kan derfor reducere marginen. Desuden kan risikoorgane bevæge sig ift. hinanden undervejs i RT-forløbet og tumor kan nogle gange skrump. Disse ændringer kan bedre visualiseres på MR billeder og den daglige RT kan tilpasses bedre. Endeligt gør brugen af MR det muligt at optage specielle typer af MR billeder, der fortæller om biologien i både tumor og normalvæv, hvilket kan oversættes til effekten af RT.

*Materiale*

På verdensplan er der endnu ingen steder, hvor man behandler med en 1,5 T MR-acc. Det har derfor ikke været muligt at kopiere den forberedelse som afdelingen skal igennem for at være klar til at behandle på maskinen. Ej heller workflow mhp forberedelse af - og behandling på MR-acc. I dette studie vil vi præsentere vores erfaringer omkring dette.

*Resultater*

MR-acc. er ikke færdiginstalleret på OUH, men vi forventer at behandle den første pt juli 2018. På kræftforskningsdagene har vi derfor mulighed for at præsentere vores erfaringer fra de første pt.

*Konklusion*

Med behandling på en MR-acc. forventer vi at kunne reducere det bestrålede område i pt, og dermed opnå en reduktion af strålerelaterede bivirkninger ved behandlingen. På sigt kan man måske øge stråledosis til tumor og dermed øge chancen for at pt overlever.

**Clinical trials + Organisation of treatment****Abstract title****#51 MR-Linac plan quality for high-risk prostate cancer radiotherapy****Presenting author**

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**Abstract***Introduction*

This study investigates the quality of high-risk prostate cancer radiotherapy dose plans for treatment on a 1.5T MR Linac compared to current clinical standard plans.

*Material and Methods*

Twenty consecutive patients planned with Pinnacle Auto-plan (Philips, WI, USA) and treated on standard Linacs with single arc VMAT plans to 78 Gy in the prostate and 56 Gy for pelvic lymph nodes over 39 fractions were included. A treatment plan was made for delivery on the Unity MR-Linac (MRL) in Monaco (Elekta AB, Stockholm, Sweden) with standard margins and dose constraints. Plan quality was evaluated by an oncologist as well as analysis of mean population dose volume histograms (DVH) and dose metrics.

*Results*

All MR-Linac plans were considered clinically acceptable, and DVH analysis showed an overall high similarity to dose distributions of the clinically delivered plans. Small, but statistically significant, differences were seen in risk organ doses, some favoring the clinical plans and others the MRL plans.

*Conclusion*

MRL treatment plans with current standard margins were clinically acceptable and similar in quality to the current standard. Thus, margin reductions facilitated by MR guided adaptive radiotherapy are therefore likely to improve overall treatment quality through reduced toxicity or higher allowed target dose.

**Patient involvement/late effects +  
Palliation:  
Poster #52-85**

**Patient involvement/late effects + Palliation****Abstract title****#52 Development of a patient decision aid template for use in different clinical settings****Presenting author**

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Karina Olling, Troels Bechmann, Poul Henning Madsen, Erik Hugger Jakobsen, Dorte Beth Toftdahl, Ole Hilberg, Angela Coulter, Karina Dahl Steffensen.

**Abstract***Introduction*

Shared decision making (SDM) is a key element on the agenda of today's health care system. Despite considerable interest from policy-makers, health care professionals and patients, SDM is not yet routine practice in clinical encounters. Health care professionals report barriers such as lack of skills and lack of decision support. Patient decision aids (PtDAs) have shown to be an effective and reliable support in the dialogue between patient and health care professionals. The aim of this study was to develop and test a patient decision aid template that could be adapted to different clinical encounters.

*Methods*

A systematic development process guided by the International Patient Decision Aid Standards (IPDAS) model was adopted and collaboration with a design school was established. Scope and purpose of prototypes were defined, steering groups were established and a PtDA template was designed. Alpha testing was conducted by structured interviews with patients and health care professionals.

*Results*

In the alpha test, 39 patients and 24 health care professionals participated. Patients and health care professionals rated the PtDA highly for usability and acceptability and the PtDAs were found suitable for preparing patients to make preference-sensitive decisions.

Qualitative findings were used to refine the PtDA.

*Conclusion*

Using a systematic process and high user involvement we developed a PtDA template and two prototypes that meet the IPDAS criteria. Testing of the PtDA prototypes showed that the template can be adapted to other clinical settings without affecting the quality of the PtDA.

Next step is to field test these prototypes with larger groups of patients and professionals, and to test additional prototypes based on the PtDA template in different clinical settings.

The PtDA template will be made available in a web-based "build-your-own-PtDA" software platform, making development of PtDAs more accessible for all health care professionals.

**Patient involvement/late effects + Palliation****Abstract title****#53 Shared decision making in decision on adjuvant radiotherapy for early stage breast cancer patients****Presenting author**

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**Abstract***Introduction*

The absolute reduction in the risk of relapse following adjuvant radiotherapy in early breast cancer can vary in patients according to prognostic factors. In this situation it is key that health care professionals are able to communicate information about benefits and risks in a balanced way. Shared decision making (SDM) using a patient decision aid (PDA) intends to help the patient to make a decision whether or not to receive radiotherapy. The aim of this study is to test whether a PDA can facilitate the involvement of patients and doctors in SDM.

*Materials and methods*

We are planning a multicenter study, where the doctors are randomized to use or not to use the developed PDA informing the patients about benefits and risks receiving adjuvant radiotherapy. The study is planned to include 300 patients offered adjuvant radiotherapy after breast-conserving surgery for T1-2, N0-N1mi, M0 disease. The PDA is developed in collaboration with participating radiotherapy centres, patient representatives and Centre for Shared Decision Making.

*Results*

The primary endpoint testing the involvement of patients in the decision process about their own radiotherapy will be evaluated using the 9-item SDM Questionnaire (SDM-Q-9). Furthermore, we will test how the developed PDA will affect the fear of recurrence using FCRI-SF as well as the overall satisfaction with the decision using the decisional conflict scale and the Decisional regret scale before and at 6 month after inclusion.

*Conclusions*

The study will be conducted on behalf of the Danish Breast Cancer Cooperative Group Radiotherapy Committee and planned to start ultimo 2018. In the start-up phase of the study, courses in SDM will be arranged several places in the country in collaboration with Centre for Shared Decision Making. These courses are supported by a grant from the Danish Comprehensive Cancer Center, to develop a group focusing on SDM in radiotherapy of breast cancer.

**Patient involvement/late effects + Palliation****Abstract title****#54 Shared decision making in care for the gynecologic cancer patient****Presenting author**

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**Abstract***Introduction*

Treatment of recurrent ovarian cancer is complex and may involve surgery, chemotherapy or surveillance options that should be discussed with patients to reach a shared decision.

This project aims to develop and test a patient decision aid (PDA) to facilitate shared decision making (SDM) in treatment planning of the ovarian cancer patient with relapse and furthermore, to evaluate SDM implementation methods

*Material & Methods*

Development, testing, evaluation, and implementation of a PDA for women with relapsed ovarian cancer will be performed at three hospitals in Denmark. The test phase will include; 1) Alpha test: Patients and clinicians are interviewed based on a structured interview guide based on internationally validated questionnaires used to assess, to what extent the PDA prepare the patient to make a decision. 2) Betatest: Validated outcome measures, such as SDM-Q9, SDM-Q-DOC, OPTION and CollaboRATE will be used to assess patients and doctors experiences of SDM in consultations with patients experiencing a disease relapse at baseline before introduction of the PDA (Betatest 1) and after the use of the PDA (Betatest 2)

*Results*

Based on an existing generic platform we have developed a PDA for platinum-sensitive as well as platinum-resistant relapse. The patient-clinician conversation in which the PDA is used consists of 5 steps: 1) The purpose of the PDA is presented 2) The patient is informed of the available treatment possibilities 3) The patients personal preferences is identified, what is important/concerns the patient 4) Patient's options and harms/benefits of each option are reviewed 5) A shared treatment decision is made with the patient

*Conclusions*

The project results are intended to be disseminated on a national level through the Danish Gynecological Cancer Group for the benefit of other cancer patients. The generic PDA template can also be adjusted and used to develop new tools for other clinical decisions within Danish healthcare.

**Patient involvement/late effects + Palliation****Abstract title****#55 Can the use of Patient-Reported Outcome Measures improve follow-up of ovarian cancer patients? PROMova, a national research project****Presenting author**

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**Authors**

Coulter A, Hjøllund NHI, Jensen PT, Steffensen KD

**Abstract***Intro*

Around 400 women are diagnosed with ovarian cancer (OC) each year. Despite excellent response to chemotherapy 80-85% of patients (pt) will relapse. In 2015, major changes in follow-up (FU) after treatment were initiated. Routine monitoring was considered ineffective and FU altered. PROMs are questionnaires designed to improve the focus on pt' needs and symptoms, but little is known about their use during FU. This study aims to assess the feasibility of using PROMs during FU as a means of incorporating pt' knowledge, needs and preferences to create an individualized FU.

*Methods*

OC pt (target N=300) who have completed first line treatment are being recruited. Pt are asked to complete PROMs every 3 months for 2 years and every 6 months the 3th year. All questionnaires are distributed by AmbuFlex, which creates a graphical overview of responses for easy clinical use. Color codes are used to graduate the severity of the PROM feedback with none, moderate and severe symptoms indicated by green, yellow and red, respectively.

*Results*

Nearly all oncology departments in Denmark participate in PROMova. Recruitment is in progress with 150 pt recruited. To date, we have experienced that PROM can be used to detect recurrence and to monitor pt quality of life and symptoms. A pt example: at baseline, when entering FU all her PROM answers were green indicating no symptoms. The next PROM assessment showed multiple red answers indicating that the pt had developed severe multiple symptoms. Shortly after this PROM assessment, recurrence was detected and treatment was initiated. By the third PROM assessment the severity of the symptoms had improved and most answers were green again, indicating that treatment effect.

*Conclusion*

The use of PROMs appears useful for detection of both recurrence and of symptoms that otherwise might be undetected. If PROMs are used as a dialogue tool during consultation improved communication, pt centered care and pt experiences is likely possible.

**Patient involvement/late effects + Palliation****Abstract title****#56 Development of a patient decision aid to support ovarian cancer patients' choice or decline of CA125 monitoring****Presenting author**

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**Authors**

Kargo AS, Coulter A, Jensen PT, Steffensen KD

**Abstract***Intro*

Each year in Denmark 400 women are diagnosed with ovarian cancer (OC). The majorities are diagnosed with advanced disease, and 70-80% will experience relapse with only limited curative potential. CA125 is a biomarker that can be detected in serum, and CA125 relapse can often be detected months before a relapse is visible by imaging. Early initiation of treatment for relapse based on increasing levels of CA125 alone does not improve survival. Danish Health Authorities recommend that personal preferences should be taken into account prior to initiating CA125 monitoring. Patient decision aids (DA) can facilitate shared decision making and help patients (pt) better understand the pros and cons of a specific intervention and furthermore, engage pt in the difficult decision whether to have CA125 measurements performed during their follow-up (FU). The aim is to develop and validate a DA to help pt decide on CA125 monitoring during FU. Here results from the alpha test will be presented.

*Methods*

Development of the DA was conducted in close collaboration with clinicians, designers, OC pt, and representatives from patient organization, KIU. Step 1: A draft DA was produced and discussed with a focus group of former OC pt. The DA was amended following their input. Step 2: DA alpha test with OC pt using a structured interview guide. Step 3: The DA was slightly altered, and is now in real-time beta testing.

*Results*

The alpha test showed (N=14) that pt had a good understanding of the information provided in the DA. In total, 10 indicated that the DA helped clarifying what was important and helped asking questions to their doctor. 12 agreed that the DA prepared them to make a better decision and helped them reflecting on their concerns regarding CA125.

*Conclusion*

The DA was found useful in decision making regarding CA125 monitoring. The majority indicated that the DA was helpful in clarifying their concerns and would be helpful in making a preference sensitive decision.



**Patient involvement/late effects + Palliation****Abstract title****#57 Patient involvement in comprehensive cancer surgery: a qualitative study****Presenting author**

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**Authors**

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**Abstract***Introduction*

Although patient involvement represents a positive paradigm shift, the concept seems challenging to health professionals and healthcare as such. On this background we investigated possibilities and limits for patient involvement in cytoreductive surgery (CRS) and hyperterm intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis.

*Methods*

During 2016-17, data was generated in two surgical university hospital departments. The material consisted in research interviews with health professionals, patients, and relatives, and observations of meetings, rounds, care situations, and other interactions. The interviews followed a semi-structured guide and were analyzed using meaning condensation.

*Results*

Eight female and seven male patients, and eight relatives, participated in 31 interviews and 37 observations. Furthermore four surgeons and five nurses participated in two focus group interviews.

We found that a primary, shared goal was to complete treatment the best possible way and improve survival. In the patients' understanding, CRS and HIPEC represented the only possibility for long term survival and it was vital to be candidates for treatment. This circumstance put the patients under considerable mental pressure during their clinical evaluation, and also affected their ability to take in information. Furthermore, the pathway was experienced complex, which in some cases resulted in patients trying to coordinate transitions themselves.

*Conclusions*

In colorectal- and ovarian cancer, comprehensive surgical pathways challenge the boundaries for patient involvement. This may cause transfer of decisions to health professionals and inexpedient use of patients' time and energy. To promote patient involvement, we suggest that patients and relatives are supported in posing questions, assisted in creating overview of their treatment pathway, and offered sufficient symptom management. In addition, coherent transitions need to be furthered.

**Patient involvement/late effects + Palliation****Abstract title****#58 Intensifying lung cancer surveillance. Development of a web-based Patient Reported Outcome application for a multicenter randomized trial in Denmark****Presenting author**

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**Abstract***Introduction*

Progressive advanced lung cancer has a poor prognosis which can quickly worsen the performance status and make the patient unfit for further treatment. Two recently published randomized studies have found both improved overall survival and health-related quality of life in cancer when adding weekly internet based self-reporting to the planned follow-up.

We are preparing a national randomized study in Denmark to test if weekly web-based surveillance through a Patient Reported Outcome(PRO) application can improve survival in lung cancer. A predefined algorithm will alert the clinician in case of symptom development between scheduled follow-up visits.

*Materials and methods*

An initial literature review will suggest approaches for the selection of disease specific PRO items and methods to define the alert threshold algorithm. We will describe the plan to confirm that the chosen approach is reliable and to calibrate the alerting mechanism. This will include an analysis of historical PRO data on Lung cancer patients treated in the Department of Oncology, Herning, matched with the cancer development. The software programming and setup will include several clinical and logistic decisions that will be sought identified and handled in the planning stage. In the final phase, we will identify possible unpredicted challenges through a pilot feasibility study on 15 patients.

*Results*

We will systematically describe the progressing phases to develop the final version of the application. The phases have been divided into; Selection of PRO items, defining the threshold algorithm, establishing the technological logistics and feasibility testing of the app.

*Conclusions*

We will present the overall methodology behind the ongoing development of the app ready to use in the randomized trial.

**Patient involvement/late effects + Palliation****Abstract title****#59 Patient-reported outcomes supporting an individualized follow-up after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. A study protocol****Presenting author**

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**Abstract***Objectives*

Patient reported outcome (PRO) have gained increasing importance as a method to evaluate postoperative outcomes. PRO is considered a useful instrument to screen for physical, functional and psychosocial problems after treatment, monitor disease progression or therapeutic response, improve communication, and heighten the awareness of patient's health related quality of life (HRQoL). The aim was to develop and evaluate an individualized cancer follow-up increasing patient involvement by focusing on patient's need, activation and HRQoL supported by PRO.

*Method*

In a clinical case-control trial from 2017-2019, patients are continuously treated with cytoreductive (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and followed in the out-patient clinic at 3, 6, 12, 18, 24, 36, 48 and 60 months postoperatively. Both CRS+HIPEC procedures and the follow-up are performed by the same consultant surgeons.

Within the study period, consultations are completed without PRO the first year thereby serving as "controls"; whereas consultations the second year are based on PRO, thus composing the intervention aiming to increase patient involvement. By an electronic system, PRO data are visually presented for the consultant, and with this as the underlying basis the consultation is performed. Outcomes as patient's need, involvement, activation and HRQoL, are assessed shortly after each consultation using The Patient activation measurement (PAM), the European Organization for Research and Treatment of Cancer (EORTC) and Generic questions concerning patient involvement. Measurements of outcome differences are compared between the two groups "controls" and "interventions".

*Conclusion*

It is expected that the intervention using PRO as the basis of an individual consultation will increase patient involvement by identifying patient's need, accede patient activation and consequently improve HRQoL.

**Patient involvement/late effects + Palliation****Abstract title****#60 Patient-reported quality of life in lung cancer: - The use of patient reported outcomes (PROs) as performance indicators****Presenting author**

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Odense Patient data Exploratory Network (OPEN), Odense University Hospital/Institute of Clinical Research, University of Southern Denmark

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**Abstract***Introduction*

For many years, treatment of lung cancer in Denmark has been audited on an annual basis using national performance indicators via the Danish Lung Cancer Registry (DLCR). However, data in DLCR give no information from the patients' perspective on the life lived with lung cancer. A well accepted way to gain information about patients' symptoms and quality of life is through the collection of patient reported outcomes (PROs). In this study, we wished to examine the feasibility of a nationwide collection of these PROs in a lung cancer population. Through analyses of the PROs collected, together with data from DLCR, we wished to develop a model, which could convert PROs into measures of quality in the treatment of lung cancer.

*Materials and methods*

The 7,295 patients registered in DLCR from 1 October 2013 until 30 September 2015 who had received treatment, were eligible for inclusion. They were asked to complete the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-LC13 questionnaires at least four times within the first year after diagnosis (before treatment, and then 3, 6 and 12 months later). Information about the patients' socioeconomic position was obtained from Statistics Denmark.

*Preliminary results*

At least one questionnaire was completed by 4,229 patients (58%), and 3,066 patients did not respond to any of the questionnaires. Responders and non-responders differed significantly on almost all variables; the responders were generally in a better health state. Patient characteristics (cancer stages, survival, socioeconomic position, etc.) were more comparable when patients were divided in groups according to their treatment.

*Conclusion*

Collection of PROs is possible in a national setting, and import to a clinical database is feasible. The next step in our study is to develop a performance indicator from the PROs collected, so that benchmarking of PROs across regions in Denmark will be possible.

**Patient involvement/late effects + Palliation****Abstract title****#61 The impact of age and comorbidity on effect of treatment, adverse effects and Quality of Life in Danish lung cancer patients receiving immunotherapy****Presenting author**

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**Abstract***Introduction*

In Denmark as well as worldwide lung cancer remains the leading cause of cancer related deaths. Comorbidities often accompany lung cancer and most lung cancer patients are over 70 years when diagnosed. Immunotherapy (check-point inhibitors) has recently shifted the treatment paradigm concerning incurable advanced/metastatic non-small-cell-lung cancer (NSCLC). It was approved for use in Denmark even though the large phase III studies didn't include patients (in a large number) over the age of 65 or patients with significant comorbidity despite the fact that these patients represent the majority of 'real life' patients.

*Materials and methods*

The Ph.D. project is part of the Elite Center AgeCare (Academy of Geriatric Cancer Research) at the University Hospital of Odense. 'Real life' data for NSCLC patients treated with immunotherapy will include:

- 1) Retrospective data from all stage IV lung cancer (NSCLC) patients treated with check-point inhibitors at the department of oncology in Odense during the period of 2015-17.
- 2) A prospective study including around 150 patients with stage IIIB-IV NSCLC patients treated with checkpoint inhibition. Baseline MRI scans screening for brain metastasis and extended CT-scans screening for deep venous thrombosis of the lungs and lower extremities will be performed. Comorbidity screening tools will be performed at baseline. Blood samples will be analyzed in order to identify predictive and prognostic biomarkers at baseline, during treatment and at follow-up and validated Quality of Life questionnaires (EORTC-QoL-30 and Euro EQ-5D-5L) will be performed.

*Conclusion*

The project will contribute with new knowledge on 'real life' NSCLC patients treated with immunotherapy which might lead to a more optimal treatment course for the individual patient and a better management of adverse events in the elderly/and or comorbid NSCLC population .

**Patient involvement/late effects + Palliation****Abstract title****#62 Quality of life and short-term side effects in non-small cell lung cancer patients treated with two different regimens of palliative thoracic radiotherapy****Presenting author**

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**Abstract***Introduction*

The aim of this study was to examine quality of life and short-term side effects in patients with advanced non-small cell lung cancer (NSCLC) treated with thoracic radiotherapy with palliative intent (PTR). The patients were treated with two different radiotherapy regimens, 30 Gy in 10 fractions and 39 Gy in 13 fractions, respectively.

*Materials and methods*

From August 2016 to March 2018, 36 patients with advanced NSCLC referred to PTR at the Department of Oncology at Odense University Hospital were included in this study. The EORTC QLQ-C15-Pal and QLQ-LC13 was used to assess QoL and respiratory symptoms. The questionnaires were completed at baseline prior to PTR, two and five weeks after completion of PTR. The repeated measures ANOVA was used to compare changes of the QLQ-C15 and QLQ-LC13 scores between the two groups. A p-value of  $<0.05$  was considered as statistically significant.

*Results*

No significant difference in changes of QoL and respiratory symptoms were found between the two groups. In patients receiving 39 Gy in 13 fractions global QoL and appetite loss deteriorated significantly from baseline to 5 week follow-up. In the group of patients receiving 30 Gy in 10 fractions, no significant changes in any of the QLQ-C15 and QLQ-LC13 scores were found at any follow-up.

*Conclusion*

In patients with advanced NSCLC treated with PTR, respectively 30 Gy in 10 fractions and 39 Gy in 13 fractions, no difference in changes of QoL was detected. Due to challenges with patient recruitment and compliance, the study population eventually became small, making interpretation of the results difficult.

**Patient involvement/late effects + Palliation****Abstract title****#63 Pre-treatment weight loss increases risk of death prior to 4th cycle of anti-neoplastic treatment in patients with inoperable non-small cell lung cancer (LUCANU-1)****Presenting author**

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**Abstract***Aim*

To assess the risk of death before 4th cycle of systemic treatment in relation to pre-treatment weight loss in patients with newly diagnosed inoperable non-small cell lung cancer (NSCLC).

*Method*

Patients with NSCLC were prospectively followed from the 1st until 4th cycle of systemic anti-neoplastic treatment (chemotherapy or immune-checkpoint inhibitor). Pre-treatment weight loss was self-reported. Patients' risk of death was calculated as odds ratio and chi-square test.

*Results*

A total of 37 out of 60 patients reported loss of body weight prior to treatment start. Mean pre-treatment weight loss was 4.8 % (range 0.4-14.7 %) and 22 of the patients had lost greater than or equal to 2.5 %. Nine patients died prior to 4th cycle of treatment, eight of whom had lost  $\geq 2.5$  % body weight prior to treatment start. The risk of death prior to 4th cycle of treatment were 4.57 times higher in patients with pre-treatment weight loss ( $\geq 2.5$  %) compared to patients without or  $< 2.5$  % pre-treatment weight loss ( $\chi^2=12.43$ ,  $p<0.001$ ).

*Conclusion*

Pre-treatment weight loss ( $\geq 2.5$  %) increases the risk of death prior to 4th cycle of systemic anti-neoplastic treatment in patients with NSCLC.

**Patient involvement/late effects + Palliation****Abstract title****#64 Does platinum-based chemotherapy given concomitantly with radiotherapy increase the risk of cardiac toxicity in definitive treated non-small cell lung cancer****Presenting author**

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**Abstract***Introduction*

The present standard of care for locally advanced non-small cell lung cancer (NSCLC) patients (pts) in good performance status (PS) is definitive chemo radiotherapy (RT). The present concomitant chemotherapy (CC) is platinum-based chemotherapy (CPC). Little is known about the late side effects of RT + CPC. Cardiac toxicity (CT) is expected to be one of them. There are no studies analyzing, the risk of developing CT after CPC-RT compared with RT alone or RT with other radio-sensitizing agents. In this study development of a cardiac event (CE) (eg ST elevations myocardial infarction (STEMI), non-STEMI, pulmonary embolus, heart failure, sudden death, pericardial effusion, supraventricular- and ventricular arrhythmia,) is defined as a surrogate marker of cardiac toxicity.

*Materials & methods*

From 2007 to 2012 309 pts were treated with definitive RT at our institution. Some of the pts were treated with CC. Pts were treated with 60 Gy/30 fractions (F) or 66 Gy/33 F. Patient files were retrospectively reviewed for CE defined as an event occurring in the follow up period. Some pts were lost for follow up to other hospitals with no access to their files. These pts were classified as no CE occurred (n=19). The pts were divided into two groups: Group 1 receiving RT + CPC and group 2 who received RT alone or RT plus other radio-sensitizing agents.

*Results*

The data were collected in April 2018. The mean survival was 36 months (range 1.6-130 months). 109 pts were treated in group 1 and 200 pts treated in group 2. Of all pts 27% had a CE (n=83). There was no difference between the two groups, 28 pts (26 %) in Group 1 and 55 pts (27 %) in Group 2 had a CE. The most frequent CE was pulmonary embolus and supraventricular arrhythmia.

*Conclusion*

CRT is part of the standard treatment for NSCLC. NSCLC pts treated with CPC were not at higher risk of developing cardiac toxicity defined as having a CE in this retrospective study compared to pts treated with definitive RT.



**Patient involvement/late effects + Palliation****Abstract title****#65 Quality of Life Research Center, Department of Haematology, Odense University Hospital****Presenting author**

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**Abstract***Introduction*

Improved treatment has in some cancer types led to transformation of life-threatening illness into chronic disease. Thus, the years lived with cancer have increased, which, in turn, highlights the need for focus on health-related Quality of Life (HR-QoL) issues. Therefore, a Quality of Life Research Center was established in 2017 at the Department of Haematology, Odense University Hospital (QoL Research OUH). The aim is to conduct independent QoL research projects and to assist clinical trials in researching factors affecting HR-QoL.

*Materials and methods*

QoL Research OUH offers 1) development of subprotocols (methods, statistics and interpretation of results) for collection of QoL data in clinical trials and 2) management of quantitative (patient reported outcomes (PROs), surveys) and/or qualitative (interviews, participant observations) data collection methods. For each study, a cooperation contract is drawn up, specifying the tasks and obligations of QoL Research OUH, including agreements on financing, affiliation, publishing. QoL Research OUH is a non-profit organization. See more at <http://en.ouh.dk/research/quality-of-life-research-center-ouh>.

*Results*

QoL Research OUH currently manages QoL data collection in five Nordic phase II hematological multi-center clinical trials besides affiliation to the world's largest nation-wide population-based cohort-study on QoL in Danish multiple myeloma patients. Collaboration in three more multicenter clinical trials is in the pipeline.

*Conclusions and perspectives*

To deliver credible QoL data thorough planning is needed. Thus, a cross-disciplinary and interdisciplinary QoL research center has been established. QoL Research OUH contributes to systematic and evidence-based collection of QoL data through quantitative and qualitative methods. The vision is to collaborate on QoL data within National and International cancer study groups.

**Patient involvement/late effects + Palliation****Abstract title****#66 Health-related quality of life in transplant non-eligible newly diagnosed multiple myeloma patients treated with melphalan/prednisolone plus either thalidomide or lenalidomide; results of the HOVON87/NMSG18 study****Presenting author**

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**Abstract***Introduction*

In the HOVON87/NMSG18 study transplant non-eligible, newly diagnosed multiple myeloma patients were randomized between melphalan/prednisolone plus either thalidomide or lenalidomide for nine induction cycles, followed by thalidomide or lenalidomide maintenance (MPT-T or MPR-R). The study showed comparable efficacy of treatment arms (Zweegman et al., Blood 2016). The aim of this study was to evaluate the health-related quality of life (HRQoL) results.

*Materials and methods*

EORTC QLQ-C30 and EORTC QLQ-MY20 were used for HRQoL measurement. The patients answered the questionnaires at baseline, after 3 and 9 induction cycles and after 6 and 12 months of maintenance. HRQoL results were evaluated according to previously published levels of minimal important difference.

*Results*

613 of the total of 637 randomized patients participated in the HRQoL reporting. Patient drop-outs reduced the number of patients completing the therapy to 15% patients in the MPT-T and 33% in the MPR-R group. All patients reported clinically meaningful improvement in global QoL, physical, role and emotional functioning, fatigue, pain, C30 summary score and future perspective. In addition, the MPT-T treated patients reported less insomnia. The MPR-R treated patients reported clinically relevant better cognitive functioning, less constipation and side effects of treatment than patients treated with MPT-T, and the MPT-T treated patients reported clinically relevant less pain, insomnia and diarrhoea than patients treated with MPR-R.

*Conclusion*

HRQoL during treatment is important, especially when treatment efficacy is comparable. MPR-R and MPT-T both demonstrated improvements in eight HRQoL domains, whereas side effects to treatment were reported differentially; an important knowledge for shared decision making. For interpretation of the HRQoL results patient drop-out rate must be taken in account, and a HRQoL study design with focus on minimization of missing data is recommendable.

**Patient involvement/late effects + Palliation****Abstract title****#67 Physical function, activity and quality of life in patients with tumor-prostheses of the lower extremities after sarcoma treatment. An exploratory cross-sectional study along with validation of the Musculoskeletal Tumor Society Score (MSTS)****Presenting author**

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**Abstract***Introduction*

Functional outcome after limb salvage procedures for bone sarcomas using tumor prostheses is sparsely described. It is often categorized using then International Classification of Functioning (ICF). Within ICF functional outcome is divided into "Body function" (e.g. strength, ROM) and "Activity&Participation" (e.g. walking capacity, ADL, workability). Few and small descriptive studies have evaluated these types of parameters.

Currently the Musculoskeletal Tumor Society (MSTS) score is the most used score to assess functional outcome, however, it is uncertain whether this score fully covers the challenges experienced by this patient group. The clinimetric properties of the MSTS score are poorly explored e.g. for patients with bone sarcomas only one study exist evaluating test-retest reliability, internal consistency and discriminant validity.

The purpose of this study is to explore what types of activities and physical function patients with tumor-prostheses find difficult to perform and evaluate physical function, activity, ADL, and QoL compared to healthy controls. Secondly, the purpose is to validate the MSTS score.

*Methods*

We will apply a cross-sectional study design including patients having tumor prosthesis implanted at Rigshospitalet 2006-2016 and healthy controls.

*Parameters tested*

Isometric muscle strength, pain (VAS), Six-Minute Walk Test, Timed up and down stairs, ADL-Q, Patient specific functional scale, MSTS score, QLQ-C30. The MSTS will be tested for interrater reliability, internal consistency, content and construct validity.

*Perspective*

This study will provide insights that may contribute to optimize postoperative rehabilitation for patients with bone sarcoma. Validation of the MSTS is needed for clinicians to interpret the sum score.

**Patient involvement/late effects + Palliation****Abstract title****#68 Systematic review of the impact of socioeconomic, demographic and religious factors on quality of life in ostomized colorectal cancer survivors****Presenting author**

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**Abstract***Background*

The formation of a fecal stoma may be necessary to obtain surgical radicality in colorectal cancer (CRC) patients but will substantially impact the health-related quality of life (HRQoL) in about 20% of cases. Little is known about patient-related risk factors for reduced HRQoL in ostomates and we decided to review the current literature on socioeconomic, demographic and religious risk factors for reduced HRQoL in CRC survivors with an ostomy.

*Methodology*

The databases Pubmed, Embase, CINAHL, PsycINFO and Cochrane Library were systematically searched. Two independent reviewers extracted, and quality assessed eligible publications. Studies assessing HRQoL with a validated questionnaire at least 6 months after surgery for colorectal cancer were included if statistical analysis was performed on the impact of socioeconomic, demographic and/or religious factors on HRQoL as either primary or secondary outcome.

*Results*

Eligible studies were predominantly small retrospective cohorts. Several studies found that both generic and stoma-specific HRQoL was lower in women than in men. Age showed equivocal results as some studies found younger patients had lower HRQoL than older patients, some concluded the opposite and yet others found no difference. Subdivision into age groups differed widely. Most studies found that socioeconomic factors did not affect HRQoL while others found lower education and not being employed correlated to reduced HRQoL. How these factors were categorized also varied widely.

*Conclusions*

The impact of socioeconomic, demographic and religious factors on HRQoL in ostomates has only been sporadically investigated in the past and this is to our knowledge the first review of the literature regarding the subject. We found HRQoL in women was reduced more than in men but conclusions regarding other factors were difficult due to varying results and varying categorization impeding the comparison. Further research in this subject is much needed.

**Patient involvement/late effects + Palliation****Abstract title****#69 Cognitive function after radiation therapy for primary brain tumours: benign tumours and low grade gliomas****Presenting author**

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**Abstract***Aim*

To assess cognitive function in patients with a primary brain tumour treated with radiation therapy (RT) to generate radio-sensitivity and volume effect parameters for prediction of cognitive dysfunction.

*Background*

After neurosurgery, RT is the main treatment for primary brain tumours. The extent of RT induced changes in cognitive function and radio-sensitivity of the brain is unknown. RT with protons instead of photons spares the healthy brain tissue more and is believed to reduce the risk of cognitive dysfunction. There is modest knowledge on which parts of the brain we need to spare, to prevent cognitive dysfunction.

*Methods*

Two studies are currently running: A cross sectional study assessing cognitive function in patients with brain tumours who received surgical resection with or without RT. 104 patients treated between 2006 and 2016 at Aarhus University Hospital was included. This is now followed up by a longitudinal nationwide study that has included 50 brain tumour patients from the four neuro oncology centres in Denmark. The patients underwent neuropsychological assessment with standardized tests. The correlation between cognitive scores and RT dose-volume parameters to specific areas in the brain will be tested.

*Results*

In the cross-sectional study, 95 patients had been tested. 66 had received RT (RT+) and 29 had not (RT-). Mean age was 54.7 years with an average time since diagnosis of 7.8 years. Compared with normative data, lower average scores were observed for the entire group on memory, processing speed and executive function: HVLT-total ( $p < 0.001$ ), HVLT-delayed ( $p < 0.001$ ), PASAT ( $p < 0.001$ ), and Stroop ( $p < 0.001$ ). Further indication of lower scores was noted for TMT-B ( $p = 0.06$ ), and Coding ( $p = 0.07$ ).

*Conclusion*

Long-term cognitive impairment was evident in majority of patients treated for brain tumors. Our results indicate that radiotherapy has detrimental effects on cognitive functions.

**Patient involvement/late effects + Palliation****Abstract title****#70 Elevated mean fractional exhaled nitric oxide and radiation pneumonitis in patients with non-small cell lung cancer****Presenting author**

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**Abstract***Introduction*

Radiation pneumonitis (RP) is a potentially fatal side effect of thoracic high-dose radiation therapy (HDRT). The aim of the study was to investigate the correlation between the grade of symptomatic RP and the mean fractional exhaled nitric oxide (FeNO) during and after HDRT in patients with non-small cell lung cancer (NSCLC).

*Materials & methods*

A total of 50 patients with NSCLC referred to HDRT were enrolled. FeNO were measured before-, weekly during six weeks of-, one month- and every third month after HDRT until the one-year follow-up. The mean FeNO was calculated using the arithmetic mean of performed baseline and weekly measurements during HDRT. Adverse events were described using the Common Terminology Criteria for Adverse Events version 4.0. Statistical analyses included demographics, dosimetric factors, pulmonary function tests (PFTs) and mean FeNO differences. Smoking and steroid treatment during HDRT were registered.

*Results*

Of the 50 patients included, 42 completed HDRT. RP was diagnosed in 24 patients, 23 patients with grade 2 and 1 patient with grade 3. On average, RP occurred 81 days after HDRT. The mean FeNO for patients with RP was 15.0 ppb (95%CI;12.0–18.0, SD 7.1), and the mean FeNO for patients without RP was 10.3 ppb (95%CI;8.6 - 11.9, SD 3.4), significantly different between the groups (log-transf.  $p=0.01$ , 95%CI;2.3-2.6). After adjustment for smoking and steroid treatment, the difference of the mean FeNO between the groups was no longer statistically significant ( $p=0.09$ , 95%CI;0.78-26.1). There was no difference in PFTs between the groups. Neither were the dosimetric factors statistically significant between patients with and without RP.

*Conclusions*

The mean value of FeNO in patients with symptomatic RP of grade  $\geq 2$  after HDRT for NSCLC was significantly higher than in patients without RP. However, smoking and peroral steroid treatment reduce its predictive power. Neither PFTs nor dosimetric parameters were predictive for RP.

**Patient involvement/late effects + Palliation****Abstract title****#71 Patient- and observer-reported long-term scar quality of wide local excision scars in melanoma patients****Presenting author**

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**Abstract***Background*

Wide local excision of the primary tumour is the mainstay of treatment for melanoma patients. The aim of this study was to assess the patient- and observer-reported long-term scar quality after surgery using the Patient and Observer Scar Assessment Scale (POSAS) in melanoma patients, to assess the reliability and validity of POSAS, and to identify factors influencing the scar assessment.

*Materials and Methods*

This cross-sectional clinical study included 320 melanoma patients with primary tumours on the trunk and limbs. Data regarding patient, treatment and scar characteristics and functional outcomes were analysed. Internal consistency, inter-rater reliability, and convergent validity were examined. Factors influencing the patient- and observer-reported scar quality was tested in regression analyses.

*Results*

Results of the POSAS showed an overall good scar quality. The internal consistency of POSAS was good and acceptable, and the convergent validity was strong. The inter-rater reliability was only moderate. The patient was influenced by the POSAS sub-items: colour, irregularity, thickness and pain. The observer was influenced by the POSAS sub-items: vascularity, surface area, thickness, relief and pliability. Both patient- and observer-reported scar qualities were influenced by age, location, type of superficial suture, keloids and widened scars. Moreover, the patient was influenced by the scar tightness and the observer was influenced by postoperative complications, hypertrophic scars, suture marks and dog ears.

*Conclusion*

POSAS is a reliable and valid scar assessment tool. The factors influencing patient- and observer-reported scar quality differed. Knowledge of this may improve treatment and hence patient-reported scar quality.

**Patient involvement/late effects + Palliation****Abstract title****#72 Normal Tissue Complication Probability model for radiation induced mucositis of H&N cancer patients****Presenting author**

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**Abstract***Purpose*

Radiation-induced mucositis is a serious acute side effect, which can jeopardize treatment compliance and influence patient weight during treatment. The aim of this study was to develop a model to predict the risk of severe mucositis for inclusion in the overall treatment optimization during treatment planning

*Methods*

535 patients from one institution receiving curative RT for H&N cancer were included. Doses were 66, 68 or 76Gy in 33, 34 or 56fx. All patients were treated with IMRT/VMAT. Mucosal reactions were scored weekly during RT, as well as 2 and 8 weeks after RT. The highest observed score was used as endpoint and dichotomised in stage 0-2 and 3+. DVH of the extended oral cavity (Brower et al) was extracted from the TPS

Predictors available for the logistic model were the first 5 principal dose components, gender, weekly low dose chemotherapy, Nimorazole, treatment acceleration, age, smoking status, site, and volume of extended oral cavity. Parameter selection was performed using LASSO within the statistical package R. The LASSO tuning parameter was chosen using 10-fold cross validation. Confidence interval was obtained from bootstrap using 2000 replicates

*Result*

Gender, acceleration, current smoker, tumour in the vicinity of the oral cavity and the two first principal dose components were selected as predictors using LASSO. Acceleration is a well-known risk factor while the tumour position indicates an increased risk beyond the prediction related to the oral cavity dose. The risk related to dose is dominated by the PC1. The model calibration plot show good agreement. The bootstrap adjusted area under the curve (AUC) was .77 (95% CI 0.73 – 0.81).

*Conclusion*

A robust logistic regression model for prediction of radiation induced mucositis of H&N has been developed, which can be used as risk assessment of mucosal toxicity during treatment plan optimisation. The AUC value of 0.77 is significantly larger than previous published models on mucositis.



**Patient involvement/late effects + Palliation****Abstract title****#73 Implementation of swallowing structures as risk organs in national radiotherapy guidelines for H&N cancer****Presenting author**

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**Abstract***Introduction*

DAHANCA's national guidelines for head and neck (H&N) cancer radiotherapy (RT) have been available since 1990, were revised in 2013 and are currently under further revision (2018). A current major revision is the inclusion of additional swallowing organs at risk (OARs) in the dose volume constraints table. The purpose of this study was to perform the first national dummy run including swallowing organs in the optimization procedure and thus, to establish a common national understanding and awareness of the possibilities to increase the quality of dose plans to limit patients' side effects after RT.

*Materials & Methods*

All six Danish centers treating H&N cancer with RT participated in the dummy run. A CT-scan from a single patient, with pre-arranged delineations of targets and OARs, was sent to the centers. The patient had UICC7 stage III oropharyngeal cancer, and prescribed dose was 66/60/50Gy to the high-dose/high-risk/low-risk PTVs, respectively. Each center prepared a dose plan according to the future version of guidelines. Dose plans were compared and evaluated at a national workshop. The centers' experience in optimizing dose according to the new swallowing organs varied from zero to several months.

*Results*

Target volumes were covered and critical organs spared in all dose plans. However, for the swallowing organs large variations were observed with standard deviations (SD) of up to 6.6Gy (lower pharyngeal constrictor muscle, PCM) from the mean, corresponding to a dose difference of 10Gy between the lowest (35Gy) and the highest (45Gy) dose to the lower PCM. Other organs with large differences in obtained sparing were glottic (SD=5.5Gy) and supraglottic larynx (SD=5.1Gy).

*Conclusions*

The majority of the dose constraints to the OARs were respected. However, the large variations in obtained mean doses to the swallowing OARs indicates a need for additional training, exchange of experience, more dummy runs and workshops to improve treatment quality.

**Patient involvement/late effects + Palliation****Abstract title****#74 Radiation therapy of sinonasal cancer****Presenting author**

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**Abstract***Introduction*

The treatment of sinonasal cancer (snc) consists of surgery and radiotherapy with x-rays (IMRT). IMRT presents a considerable challenge because of important structures in close proximity to the tumor, and radiation of those structures is unavoidable. Subsequent damage to this normal tissue might have large impact on the patient's quality of life due to permanent late toxicity. In Denmark, proton therapy will be available by the end of 2018. Protons have different depth-dose characteristics, which makes it possible to deliver a high radiation dose in a precise location, and hereby spare normal tissue and reduce toxicity. Because of different physical properties and the limited capacity, it is of great importance to generate a model for patient selection and investigate physical aspects of treatment planning in order to establish ideal treatment protocols. This PhD project aims to evaluate both organ specific late toxicity and pattern of failure in patients treated with IMRT as well as prospectively register toxicity and outcome after proton therapy for snc. Lastly, we wish to investigate how to manage the different physical entities in proton treatment planning.

*Materials and methods*

Patients treated with radiation therapy for sinonasal cancer in Denmark in 2008-2016 are included in the studies. Toxicity after both IMRT and proton therapy are objectively assessed by specialists in ophthalmology, psychology and endocrinology. Pattern of failure analysis is performed based on fusion of dose plans and recurrence CT scans using software for deformable image registration.

*Results*

The project is approved from relevant ethics boards, and all collaboration has been established. Results are expected within the next 2 years.

*Perspective*

Normal tissue surrounding the tumors poses a significant challenge for the treatment of sinonasal cancer. Proton therapy may improve outcome of radiation therapy while sparing normal tissue and thus reduce side effects.

**Patient involvement/late effects + Palliation****Abstract title****#75 PRO-MR Linac – en systematisk, webbaseret indsamling og evaluering af patient-rapporterede symptomer (PRO) til MR Linac behandling****Presenting author**

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**Abstract***Introduktion*

I de kommende år forventes ny teknologi, MR accelerators, at ændre omfanget af stråleinduceret toksicitet under og efter strålebehandling. Den nuværende praksis indenfor stråleterapi er primært klinikervurderet toksicitet, og patienternes symptomer indsamles ikke altid systematisk. Mange forskellige behandlere er involverede i den enkelte patients forløb, og det kan være vanskeligt at følge og vurdere nyttilkomne samt eksisterende symptomer. På OUH installeres i 2018 en MR Linac. Det er væsentligt, at symptomer rapporteret af patienterne selv, er et effektmål i vurderingen af denne nye teknologi.

*Materiale og metode*

Studiet vil inkludere patienter, der skal modtage strålebehandling på en MR Linac.

Første del af studiet vil være et longitudinelt studie, hvor systematisk PRO-registrering primært vil foregå via appen MitForløb, som patienten kan tilgå via egen device/pc. Patientens symptomer kan efterfølgende ses i den elektroniske patientjournal (EPJ). Til PRO-registreringerne anvendes udvalgte symptomer fra PRO-skemaet PRO-CTCAE, som kombinerer symptomernes frekvens, sværhedsgrad og indgriben i patientens liv.

Anden del af studiet vil undersøge patientens oplevelser med MR Linac behandling samt PRO-registrering.

Endeligt undersøges hvordan de patientrapporterede oplysninger kan anvendes til en mere behovsstyret opfølgning på patientens akutte toksicitet og en screening for rehabiliteringsbehov til primær sektor.

*Forventede resultater*

Studiet forventes at undersøge, hvordan webbaserede, patient-rapporterede symptomer (PRO) kan være en integreret del af en systematisk, klinisk vurdering af effekten af MR Linac behandling – en patient-centreret symptomhåndtering under strålebehandling og follow-up baseret på behovsstyret opfølgning.

*Patientinddragelse*

Patienter inddrages i idéfasen og i feasibility studier omkring webbaseret PRO-registrering under strålebehandling.

Studiet gennemføres som et ph.d. studie og forventes påbegyndt ultimo 2018.

**Patient involvement/late effects + Palliation****Abstract title****#76 Organisatorisk brugerinddragelse i udvikling af forskningsbaseret patientinformation om protonterapi****Presenting author**

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**Authors**

Kristensen A.W., Hansen H.

**Abstract***Introduktion*

Der findes ikke erfaringer med udarbejdelse af patientinformation om protonterapi til danske patienter. Med henblik på at indsamle viden om patientperspektivet er organisatorisk brugerinddragelse anvendt i Dansk Center for Partikelterapi (DCPT) som grundlag for udarbejdelse af patientinformation. Formålet med projektet er at:

- Udarbejde forskningsbaseret patientinformation med udgangspunkt i patienters erfaringer under hensyntagen til det specielle der kan gøre sig gældende for voksne i behandling i forhold til familier med et barn i behandling.

*Materiale og metode*

Der er foretaget kvalitative semi-strukturerede interviews med 7 voksne (18-55år) og 8 familier med børn/unge i alderen 2-18 år. Interviewpersonerne har modtaget protonbehandling i udlandet inden for de seneste 2 år. Det indsamlede materiale gennemlyttes af to personer individuelt og meningskondenseres ud fra en Ricoeur inspireret analysemodel. Efter gennemlytning sammenholdes meningskondenseringer og der opnås enighed om definition af nye temaer.

Med henblik på at kvalitetssikre den forskningsbaserede patientinformation inddrages et brugerpanel bestående af interviewpersonerne, så der sikres genkendelighed mellem patienternes udtalelser og det færdige produkt.

*Resultater*

Foreløbige resultater viser, at patienter foretrækker film som medie. Filmene skal indeholde information om:

- Forskellen på behandling med protoner og fotoner, hvad protoner er samt hvornår protoner foretrækkes
  - Maskinens udseende, hvordan masken fremstilles, hvordan scanninger og behandling foregår samt årsager til ventetid før behandlingsstart
  - Hvordan og i hvilken grad bivirkninger vil påvirke patientens liv og dagligdag fremadrettet
- Desuden efterspørges information om praktiske forhold (indkøb, transport, overnatning mm).

*Konklusion*

Den benyttede metode til organisatorisk brugerinddragelse har vist sig anvendelig til at repræsentere patientperspektivet ved udarbejdelse af forskningsbaseret patientinformation i DCPT.

**Patient involvement/late effects + Palliation****Abstract title****#77 Betydningen af en terapeut fast tilknyttet Onkologisk Sengeafsnit - plejepersonalets oplevelser****Presenting author**

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**Abstract***Indledning*

Onkologisk sengeafsnit modtager patienter til hospitalsindlæggelse, med fokus på udredning og behandling af akutte problemstillinger, herunder hindring af fald i fysisk funktionsniveau. Funktionsevnevurdering, opstart af terapi samt rettidigt og fyldestgørende kommunikation med patientens hjemkommune er afgørende for et godt indlæggelsesforløb. Ergo- og fysioterapeuter spiller i dette arbejde en essentiel rolle. Med henblik på at optimere varetagelsen af disse opgaver blev en terapeut fast tilknyttet onkologisk sengeafsnit. Betydningen af ansættelsen for plejepersonalets daglige arbejde blev efterfølgende afdækket kvalitativt.

*Materiale og Metode*

Fem sygeplejersker med mindst 2 års praksiserfaring fra onkologisk sengeafsnit blev tilfældigt udvalgt til deltagelse i semistrukturerede interviews. Interviewene blev analyseret ved systematisk tekstkondensering.

*Resultater*

Sygeplejerskerne oplevede, at funktionsevnevurdering, rekvirering af hjælpemidler samt igangsættelse af terapeutisk intervention blev hurtigere iværksat.

Terapeutens opstart af tværsektoriel kommunikation i form af den tværsektorielle meddelelse (TSM) effektiviserede arbejdsgangen i forhold til forberedelse af udskrivelse, hvilket minimerede unødige indlæggelsesdøgn. Flere informanter gav udtryk for, at TSM fokus mere tydeligt var præget af vurdering af patientens funktionsevne, i modsætning til tidligere, hvor denne primært var rettet mod patientens behov for medicinsk behandling og det overordnede sygdomsbillede.

Det blev fremhævet, at en fast tilknytning af en terapeut til sengeafsnittet, som kunne deltage i møder og konferencer samt fungere som bindeled til resten af terapeutgruppen, var fordelagtig i det tværfaglige samarbejde.

*Konklusion*

Resultaterne indikerer, at en fast tilknytning af en terapeut til et onkologisk sengeafsnit opleves positivt af de tværfaglige samarbejdspartnere, særligt i forhold til vurdering af funktionsniveau, behov for hjælpemidler og udfyldelse af TSM.

**Patient involvement/late effects + Palliation****Abstract title****#78 See and treat in an outpatient setting in women aged 45 years and older with cervical dysplasia****Presenting author**

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**Authors**

Gustafson L.W, Hammer A, Petersen L.K, Andersen B., Bor P

**Abstract***Introduction*

Cervical cancer is the fourth most frequent cancer among women worldwide. In Denmark, 370 women are diagnosed with cervical cancer annually and approximately 100 women die of the disease. The sensitivity of cervical cytology decreases with age and the performance of colposcopy is low, particularly in postmenopausal women due to the retraction of the transformation zone into the cervical canal. Thus, postmenopausal women are often required to undergo colposcopy several times. The 'See and treat' approach is a combined procedure, which includes sampling of cervical cytology, HPV test, colposcopy, cervical punch biopsies, and finally a loop electrosurgical excisional procedure (LEEP), which allows women to be diagnosed and treated in one visit.

*Aim*

This project aims to investigate if the implementation of 'see and treat' in a gynecological outpatient clinic can optimize the diagnostic, clinical follow-up, and treatment of women aged  $\geq 45$  years with abnormal cervical cytology.

*Methods*

Study 1. Descriptive cohort study including women aged  $\geq 45$  years referred to four gynecologic departments in Central Denmark Region and at Aalborg University Hospital due to cervical dysplasia. We will describe the prevalence of HPV and cervical dysplasia and the agreement rate between the results of colposcopy, cervical punch biopsies, and LEEP.

Study 2. A cost-benefit analysis of the 'see and treat' approach.

Study 3. A questionnaire study aiming to explore the psychological impact, treatment preferences, socio-economic status, previous disease, and patients satisfaction with the 'see and treat' procedure using a validated questionnaire.

*Perspective*

Our results may provide evidence on how to best treat women  $\geq 45$  years with abnormal cytology, provide knowledge on patient experience, and it may lead to a more cost-effective approach. In the long run, the implementation of "see and treat" might lead to a decrease in cervical cancer incidence and mortality.

**Patient involvement/late effects + Palliation****Abstract title****#79 Patient perspectives on colorectal cancer screening after a non-cancer colonoscopy result. A qualitative study****Presenting author**

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**Authors**

Kirkegaard P, Edwards A, Andersen B

**Abstract***Introduction*

In population-based cancer screening, many screening participants with a positive screening test result have normal diagnostic follow-up investigations, and for them it is thus a 'false alarm' for cancer. The objective of the study was to explore perceptions of cancer screening among participants with normal follow-up investigations, and to identify motivations for continued screening participation.

*Materials and methods*

Semi-structured interviews with screening participants who had participated in the Danish colorectal cancer screening program with normal follow-up investigations. A thematic analysis was performed, based on an interpretive tradition of ethnography.

*Results*

The most prominent themes in the accounts were institutional and interpersonal trust, balancing risk and benefits, and perceived obligation to participate. Trust included trust in the professional skills of the healthcare professional performing the colonoscopy, and for most participants the patient-involving behavior of the was considered a cornerstone for trusting the validity of the colonoscopy result. Many participants emphasized early detection of disease as an optimal way to support effective treatment, and satisfaction with the procedure and gratitude towards the screening program for providing a thorough examination were commonly expressed. Knowing about other population-based cancer screening programs increased the sense of familiarity, and participation was considered by many a moral and social obligation given that society has devoted scarce resources to it.

*Conclusions*

The risk for 'false alarm' in screening was considered as worth taking in the pursuit of good health, also in future screening. Institutional and interpersonal trust were prominent factors in screening participants' accounts about motivation for future screening and should be identified and advanced to secure informed decision-making about screening participation.

**Patient involvement/late effects + Palliation****Abstract title****#80 Communicating detailed information about colorectal cancer screening to citizens with lower educational attainment using an electronic decision aid: a qualitative study****Presenting author**

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**Authors**

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**Abstract***Introduction*

Compared to average educational attainment citizens, citizens with lower educational attainment (LEA) less frequently take up colorectal cancer (CRC) screening, and to a lesser degree read and understand conventional screening information. The information needs of LEA citizens ranges from a clear recommendation to elaborating information. Some decision aids (DAs) are designed to support informed decision making about CRC screening participation, but none embraces diversion in information needs. The aim of this study was to develop such a DA tailored to LEA citizens.

*Materials and methods*

A prototype of the DA was developed based on the IPDAS guidelines along with LEA citizens' information needs. The online DA presented information in steps. Values clarification questions were included and answers summarized in a choice-barometer on the last page. Statistics were presented in both relative and absolute numbers. Both user testing, peer review and field testing were conducted using focus group and telephone interviews and email correspondences with LEA citizens and healthcare professionals. Data was analyzed using thematic analysis.

*Results*

The citizens found the DA easy to understand and the text of suitable length. They easily and intuitively navigated around the DA, and stated, that they felt encouraged to think about benefits and harms of CRC screening without being overloaded with information.

*Conclusions*

This DA represents a new way of communicating detailed information about CRC screening to LEA citizens, enabling citizens to make value-based decisions. Further, this work might serve as an inspiration when developing information material in other screening programs.



**Patient involvement/late effects + Palliation****Abstract title****#81 Development of evidence-based national clinical guidelines in palliative care****Presenting author**

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**Authors**

Villadsen, B; Lassen, TH.

**Abstract***Aim*

The aim of developing evidence-based national clinical guidelines is to improve the quality of specialist palliative care.

*Methods*

The guidelines are developed multi-disciplinary with more than a hundred participants, primarily nurses and doctors, from hospices, palliative departments and teams from all parts of the country. Clinical, scientific and management qualifications are a prerequisite for a successful result. The health care professionals are responsible for the clinical relevance of the content in the clinical guideline, the methodological quality is ensured by an academic consultant, and the work process is organized by a coordinator. The guidelines follow the requirements from the Danish Clearinghouse for Guidelines (CFKR). The guidelines are initially reviewed by the CFKR, followed by an external review by three methodological experts using the AGREE II instrument. Hereafter the guideline is sent to a public hearing.

*Results*

17 guidelines aimed for cancer patients in palliative care have been published (dyspnea; screening for delirium; prevention of delirium; pharmacological treatment of delirium; relatives and delirium; relief of death rattle; interventions to support families of cancer patients; treatment of lymphedema; support for teenagers to parents with cancer, screening for depression, treatment of clinical depression, pharmacological treatment of constipation, opioid pain treatment, psychosocial interventions for fatigue; exercise to alleviate fatigue; pharmacological treatment of fatigue; palliative sedation).

*Conclusion*

Throughout the nine years since the establishment of DMCG-PAL, we have shown that it is possible to develop national, multidisciplinary evidence-based clinical guidelines.

The presence of managerial, academic and clinical skills is a prerequisite to develop clinical guidelines. Participants gain skills in systematic methodology and are responsible for implementing the guideline in their own department or hospice.

**Patient involvement/late effects + Palliation****Abstract title****#82 Indkomst og uddannelsesniveau har betydning for kræftpatienters adgang til specialiseret palliativ indsats i Danmark****Presenting author**

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**Abstract***Introduktion*

I Danmark foregår specialiseret palliativ indsats (SPI) på hospitaler (palliative teams/enheder) og hospicer, og SPI er fundet værdifuld for patienter og deres pårørende. I Danmark er der begrænset viden om, hvilke patienter, der får adgang til SPI og internationale studier har vist divergerende resultater. Studiets formål var at undersøge om adgang til SPI var associeret med indkomst eller uddannelse.

*Metode og materiale*

Studiepopulationen var de 44.548 patienter, der døde af kræft i Danmark i 2010-12. Studiet var baseret på data fra Dansk Palliativ Database (national klinisk kvalitetsdatabase) og andre nationale høj-kvalitetsregistre. Logistisk regressionsanalyse (ujusteret og justeret) blev anvendt til at undersøge sammenhængen mellem adgang og hhv. uddannelse, indkomst og den kombinerede effekt af uddannelse og indkomst.

*Resultater*

Sammenlignet med patienter med grunduddannelse havde akademikere større chance for at få adgang til SPI (Odds ratio (OR) =1,7 (95%KI: 1,5;1,9)). For indkomst havde patienter i den højeste indkomstkvartil større chance for at få adgang til SPI sammenlignet med laveste indkomstkvartil (OR=1,5 (95%KI: 1,4;1,6)). Analysen af den kombinerede effekt af uddannelse og indkomst, fandt for hvert uddannelsesniveau stigende chance for at få adgang til SPI med stigende indkomst, med undtagelse af akademikere hvor adgangen var høj i både laveste (OR= 2,0; 95%KI 1,3;3,1) og højeste indkomstkvartil (OR=2,0; 95%KI1,7;2,3).

*Konklusion*

Baseret på unikke danske registre, viser dette studie, at adgang til SPI var lavere for patienter med kort uddannelse og lav indkomst. Da behovet for SPI i disse grupper må formodes at være tilsvarende eller endda højere, tyder resultaterne på, at der i Danmark er tale om betydelig social ulighed i adgang til SPI – formentlig fordi der er utilstrækkelig kapacitet, og således er det de mest ressourcestærke patienter, der er bedst til at navigere i sundhedsvæsenet.

**Patient involvement/late effects + Palliation****Abstract title****#83 Age, gender and cancer site specific HRQOL at the start of specialized palliative care - a nationwide study of 21,234 Danish cancer patients****Presenting author**

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**Authors**

Hansen MB, Ross L, Petersen MA, Groenvold M

**Abstract***Background*

Large, nationally representative studies of health-related quality of life (HRQOL) in cancer patients in specialized palliative care (SPC) are missing.

*Aims*

The aim of this study was to describe HRQOL in cancer patients at the start of SPC and to investigate how age, gender and cancer site were associated with these outcomes.

*Methods*

Data from the Danish Palliative Care Database was used in this study. We included cancer patients who completed EORTC QLQ-C15-PAL at admission to SPC from 2010 until end 2015. For these patients we calculated mean scores for the 10 HRQOL aspects according to age, gender and cancer site and performed ordinal logistic regression to test if age and gender (controlled for the effect of cancer site and gender or age) were associated with each outcome.

*Results*

21,234 patients answered EORTC QLQ-C15-PAL at admission to SPC and were included in the analyses. The average age was 68.6 years, about half were women and the most common diagnosis was lung cancer. The patients had the highest scores for fatigue, appetite loss and pain and had poor physical functioning and poor QOL. Results from the ordinal logistic regression showed that increasing age was associated with lower levels of pain and insomnia but increased risk of poor physical functioning. Women compared to men had a higher risk of nausea but lower risk of insomnia. Overall, patients with brain and central nervous system cancer had the lowest levels of symptoms/functioning problems, whereas patients with ovarian cancer had the highest levels.

*Conclusion*

The patients starting SPC were troubled by severe levels of symptoms, poor physical functioning and reduced QOL. Patients with ovarian cancer were the most troubled. Younger age was associated with higher levels of pain and insomnia but better physical functioning. Women had higher levels of nausea than men but less insomnia.

**Patient involvement/late effects + Palliation****Abstract title****#84 Incidence of surgical interventions for metastatic bone disease in the extremities: A population based cohort study****Presenting author**

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**Authors**

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**Abstract***Introduction*

Outcome after surgical treatment of metastatic bone disease in the extremities (MBDex) is known to be socio-economical beneficial and functional outcome is improved if the lesion is treated prior to complete fracture. Current study aimed at clarifying the demographics and presentation of MBDex to the orthopedic surgeon.

*Study design/methods*

Prospective cross-sectional study identifying all patients having surgery for MBDex (6 orthopedic departments) from May 2014 to May 2016.

*Results*

We identified 164 patients (168 surgical procedures / 175 bone lesions), resulting in an incidence of MBDex surgery of 48.6 lesions/million inhabitants/year. Seventy-four percent of lesions were fractured at the time of orthopedic intervention. Twenty-nine lesions represented debut of cancer and 22 lesions debut of relapse (of whom 8 patients did participate in surveillance programs that failed to detect bone metastasis). One-hundred-twenty-seven patients participated in surveillance programs that included CT-thorax/abdomen. In 47% of these cases the scans did not detect MBDex and the lesions were identified due to acute pathological fracture.

*Conclusions*

We are, to our knowledge, the first to describe a prospective population based cohort of patient having surgery for MBDex. We found that 47% of lesions were not identified on surveillance programs (in 8 patients the lesions represented debut of relapsed not detected by scans). We regret to find the the majority of patients experienced a complete fracture prior to referral for orthopedic intervention and advocate for mere focus on identifying and treat MBDex in an early stage to ensure the highest quality of life for the remainder of the patient's life.

**Patient involvement/late effects + Palliation****Abstract title****#85 Use of cannabis among cancer patients receiving palliative care – a qualitative interview study****Presenting author**

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**Authors**

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**Abstract***Introduction*

There is an increased focus on use of cannabis in a medical context, primarily for pain relief. There is only sparse information on the prevalence of cannabis use among terminal cancer patients in Denmark. An American study shows that 20-30% of patients with cancer use legalized cannabis. In Denmark, cannabis is legally accessible by a physician prescription only. A majority of terminal cancer using cannabis obtain the products from the illegal market. The purpose of this study is to collect information about use of cannabis among terminal cancer patients.

*Material and methods*

Qualitative research interviews with a semi structured interview guide are conducted. The analysis process takes three steps: naive reading, structure analysis, critical interpretation and discussion. Approximately 20 interviews are expected to provide sufficient data. Patients referred to the palliative care team at the North Denmark Regional Hospital and using cannabis for treatment will be included in the study. The patients receive oral and written information on the project and signed informed consent is obtained prior to participation. Patients who are delirious, brain damaged, moribund or suffering from dementia are excluded.

*Results*

Preliminary interview findings among the terminal cancer patients included in the study so far have revealed that the main reason for the use of cannabis is hope – hope for a cure. Some of the statements were: “That it (cannabis) can kill the cancer – that is what I am hoping for”; “we panicked to such an extent when I got the diagnosis, that we wanted to try anything in to see if I could recover”; “I want to do it all, because I want to live”. The participants further states that they do experience symptom relief, especially when it comes to sleep, unrest and pain. None of the included patients experienced side effects to cannabis.

*Conclusions*

Final study results and conclusions will be presented at Danish Research Cancer Days 2018.

**Biomarkers and diagnostics +  
Basic and translational research:  
Poster #86-108**

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#86 Circulating biomarkers in diagnosis, risk stratification, and follow-up of high grade sarcomas in adults: A Danish Sarcoma Group study****Presenting author**

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**Authors**

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**Abstract***Background*

To improve sarcoma treatment outcome one has to tackle 3 major problems; 1) how to better differentiate sarcomas from benign tumours, 2) how to better identify high risk patients, and 3) how to detect potentially curative metastasis before they become symptomatic.

*Introduction*

Tumour cells release biomarkers reflecting the biology and tumour burden of individual sarcomas into the circulation. Based on our previous research and new literature data we hypothesize that these circulating biomarkers could be diagnostic and prognostic tools as well as biological instruments to predict treatment response.

*Material and Methods*

This is a national research between the 2 specialized sarcoma centers in Denmark and endorsed by the Danish Sarcoma Group. It suggests to use the detection of inflammation biomarkers, exosome and circulating tumour DNA (ctDNA) in blood samples taken before and after treatment as well as during follow-up of all patients with localized high grade sarcomas. The aims are to answer the following questions:

- Can circulating biomarkers differentiate between benign tumours and sarcomas?
- Will the circulating biomarkers disappear from the blood after radical treatment?
- Will the persistence or reappearance of the biomarkers mark an impending recurrence?
- Is disease recurrence associated with the appearance of new biomarkers?
- Can some of the biomarkers be potential therapeutic targets?
- Can any of these circulating biomarkers predict the response to treatment?

*Perspectives*

This project would generate the largest and most comprehensive and systematic data set on biomarkers in high grade sarcomas worldwide. The results will help us to understand the relationship between inflammatory process and the biology of sarcoma progression over time together with the molecular events associated with metastasis. It will improve the diagnostic accuracy and individualize therapy based on individual molecular targets.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#87 Aarhus composite biomarker score (ACBS): A prognostic tool for inferior survival in localized high grade sarcomas****Presenting author**

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**Authors**

Aggerholm-Pedersen N, Maretty-Kongstad K, Keller J, Bærentzen S

**Abstract***Background*

The current prognostic factors are of limited value as treatment stratification tool for sarcomas. A more accurate method of identifying high risk patients is badly needed. Inflammation is one of the hallmarks of cancer, and inflammation biomarkers are excellent candidates for clinical testing.

*Material and Methods*

All patients with localized high grade bone sarcomas (BS) and soft tissue sarcomas (STS) treated in Aarhus Sarcoma Centre between 1994 and 2008 were extracted from the Aarhus Sarcoma Registry. Pre-treatment levels of albumin, C reactive protein, hemoglobin, neutrophils, and lymphocytes were collected from the patient records of 818 patients with STS and 172 patients with BS. A new composite prognostic score incorporating all 5 biomarkers (Aarhus composite biomarker score: ACBS) were constructed. The prognostic values of individual markers on disease specific survival (DSS) and overall survival (OS) was estimated using crude and adjusted Cox proportional hazard models. Adjustments were made for comorbidity as well as other prognostic factors using the Cox proportional hazard model. For validation, the STS cohort was randomly divided into a test and validation cohorts while the validation of the bone sarcoma data was done using the boot strapping statistical method.

*Results*

All individual biomarkers were prognostic for survival for both STS and BS. ACBS was significantly superior prognostic factor and could stratify patients into various risk groups also after adjusting for confounders including comorbidities. The higher the numerical value of the score (reflecting the number of abnormal biomarkers), the higher was the sarcoma-specific mortality. Statistical validation confirmed the independent prognostic value of the ACBS.

*Perspectives*

Future studies will be directed towards further validation of the score in independent international datasets and towards integrating the ACBS into the routine clinical decision of sarcoma patients.



**Biomarkers and diagnostics + Basic and translational research****Abstract title****#88 Impact of molecular heterogeneity in B cell malignancies****Presenting author**

Simone Valentin Hansen

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**Authors**

Simone Valentin Hansen (SVH), Oriane Cédile (OC), Jacob Haaber (JH), Moustapha Kassem (MK), Niels Abildgaard (NA) and Charlotte Guldborg Nyvold (CGN).

**Abstract**

Malignant blood diseases are an extremely heterogeneous entity. Precision medicine has been shown to be successful in the treatment of B cell malignancies with inhibitors of Bruton's tyrosine kinase and inhibitors of important immune checkpoints such as the programmed death protein 1. Treatment efficiency is highly dependent on the mutational landscape of the cancer and microenvironment. Thus, molecular characterization is required to implement this new generation of targeted drugs.

This project is focused on exploring the genetic background in a subset of haematological B cell malignancies. We aim to identify genes that are important for malignant transformation of B cells in mantle cell lymphoma (MCL) with the ultimate goal of identifying novel anti-cancer targets. Based on comprehensive sequencing data from MCL patients previously generated in our laboratory genes that were found to be aberrantly expressed or mutated in malignant B cells have been selected. To investigate the possible impact of these genes on malignant transformation, functional studies will be performed both on cell lines and primary patient cells. This will include modification of cells using CRISPR-CAS9 technology.

Additionally, we will characterize the molecular heterogeneity within different subpopulations of the cancer and microenvironment in patients diagnosed with B cell malignancies who were treated with novel drugs. The mutational and transcriptional status before, during, and after treatment will be explored using exome and global RNA sequencing on sorted cells. The intra-tumor heterogeneity within single patients will be characterized by global single cell RNA sequencing, and data analysis will focus on differential gene expression between the bulk sorted cell population and the single cells. We expect that these studies will add valuable knowledge about the biology and treatment efficiency of B cell malignancies, and may influence the choice of targeted therapy in the future.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#89 Tumor-infiltrating lymphocytes predicts improved overall survival after post-mastectomy radiotherapy****Presenting author**

Trine Tramm

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**Abstract***Introduction*

High level of tumor-infiltrating lymphocytes (TILs) is associated with improved recurrence free- and overall survival (OS) in especially some breast cancers (BC), and has been found to predict response to neoadjuvant chemotherapy. Our aim was to investigate the predictive value of TILs in terms of benefit from radiation therapy (RT) in a cohort of BC patients randomized to RT or not.

*Materials and Methods*

The Danish Breast Cancer Group (DBCG) 82bc cohort constitutes high risk BC patients diagnosed between 1983-89, treated with mastectomy and axillary lymph node dissection followed by adjuvant systemic treatment and randomized to +/- post-mastectomy radiotherapy (PMRT), and associated with > 20 years of clinical follow-up. In 1,011 pretreatment, tumor-containing paraffinblocks, TILs were estimated using HE staining's following international recommendations. A competing risk model, Kaplan-Meier analysis and multivariate Cox regression analysis (MVA) were used for analyzing correlations between TILs and clinical outcome.

*Results*

Using a cut-off of 30%, lead to 10.5% of patients (106/1,011) being categorized as having 'high' level of TILs. For patients with both "low" and "high" TILs values, a benefit from PMRT could be found for all clinical endpoints. The benefit of PMRT to reduce the risk of LRR was equal in the two TILs groups at 20 years, whereas a trend for greater reduction was observed for DM (11% vs. 19%,  $p=0.29$ ). A significantly greater benefit from PMRT was observed for 'high' TILs patients as compared to 'low' TILs patients with significantly improved OS at 20 years ( $p=0.045$ ). The association remained significant, when adjusting for clinical variables in MVA.

*Conclusion*

High levels of pretreatment TILs was associated with improved OS, but not with local control in a cohort of BC patients treated with PMRT. The finding may indicate that RT triggers a local immune response that induces a systemic effect outside the treatment field.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#90 Cell-free DNA promoter hypermethylation in plasma as biomarkers for pancreatic adenocarcinoma****Presenting author**

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**Abstract***Background*

Pancreatic cancer is the 4th leading cause of cancer death with a 5-year survival rate of 5-7%. Minimal invasive diagnostic and prognostic tools are lacking. DNA promoter hypermethylation is a part of early carcinogenesis and can cause inactivation of tumour suppressor genes. The aim of this study was to test promoter hypermethylation in a panel of genes from plasma-derived cell-free DNA as biomarkers for pancreatic cancer.

*Methods*

Consecutive patients with suspected or biopsy-verified pancreatic cancer were included prospectively. Patients with chronic pancreatitis were included as an additional benign control group. Methylation-specific PCR of 28 genes was applied on plasma samples. Diagnostic and prognostic prediction models were developed by multivariable logistic regression analysis.

*Results*

Patients with pancreatic adenocarcinoma (n=95), patients with chronic pancreatitis (n=97), and patients screened for, but not having pancreatic adenocarcinoma (n=27) were included. The mean number of methylated genes in the cancer group was (8.41(95% CI 7.62-9.20)) vs the total control group (4.46(95% CI 4.04-4.88)) (p<0.001). A diagnostic prediction model (age>65, BMP3, RASSF1A, BNC1, MESTv2, TFPI2, APC, SFRP1, and SFRP2) had an AUC of 0.86 (sensitivity 76%, specificity 83%). The model performance was independent of cancer stage. A prognostic prediction model for distant metastasis (SEPT9v2, SST, ALX4, CDKN2B, HIC1, MLH1, NEUROG1, BNC1) had an AUC of 0.87 (sensitivity 74%, specificity 87%). Patients with more than 10 hypermethylated genes had a HR of 2.03 (95% CI; 1.15-3.57) compared to patients with fewer hypermethylated genes.

*Conclusions*

Cell-free DNA promoter hypermethylation has the potential to be diagnostic and prognostic biomarkers for pancreatic adenocarcinoma. External validation is, however, required to substantiate the results. A validation study has been initiated.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#91 Novel DNA methylation markers show high sensitivity and specificity for blood-based detection of colorectal cancer****Presenting author**

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**Abstract***Background*

Screening for colorectal cancer (CRC) can cost-effectively reduce mortality/morbidity. The cardinal screening tools are endoscopy/fecal occult blood testing (FOBT), but both suffer from low compliance. Further CRCs only bleed intermittently, limiting FOBT sensitivity. Thus, new tests with high compliance and high sensitivity/specificity are warranted.

*Aim*

To develop and validate a minimally-invasive blood-based circulating cell-free DNA (cfDNA) approach for CRC detection, using methylation biomarkers.

*Materials and methods*

Three CRC-specific methylation markers were identified by analysis of Illumina 450K methylation array data from >4,000 samples. By digital droplet PCR (ddPCR) their performance was tested in plasma from 113 symptomatic CRC patients and 86 colonoscopy negative controls on a fixed input of 4,500 cfDNA copies/ddPCR reaction. The performance was independently validated in plasma from 143 symptomatic CRC patients, 41 adenoma patients and 121 colonoscopy negative controls. All non-CRC individuals were FOBT positive, included from the DK screening program.

*Results*

The three markers had a combined sensitivity of 81% in the first cohort. Sensitivity increased with stage (65%, 85%, 78%, and 83% for stage I-IV). Findings were replicated in the independent validation cohort that showed 84%'s sensitivity (79%, 82%, and 91% for stage I-III). Sensitivity for adenomas only reached 15%. Specificities were 99% and 93% in the two cohorts. Importantly, our analyses show that it is essential to analyze  $\geq 4,500$  cfDNA copies to reach the reported sensitivities and confidentially call samples negative.

*Conclusion*

We have developed a blood-based test with great potential for CRC detection; both as stand-alone screening test and as supplement to existing endoscopy/FOBT programs, where it can be offered to those declining participation. It can also be used for triaging FIT-positive screening individuals to reduce the number of downstream colonoscopies.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#92 Whole blood gene expression profiling in patients undergoing colon cancer surgery identifies differential expression of genes involved in immune surveillance, inflammation and carcinogenesis****Presenting author**

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**Abstract***Introduction*

Surgery is included in any curative treatment strategy for solid cancers, and growing evidence supports that the stress, related to cancer surgery, might increase the risk of residual cancer in otherwise curatively treated cancer patients. The aim of this study was to identify changes in transcription of genes involved in immune surveillance, immune suppression, and carcinogenesis after surgery in a cohort of patients undergoing curatively intended laparoscopic colon-cancer surgery.

*Materials and methods*

Patients undergoing elective, curatively intended laparoscopic surgery for colon cancer stage I-III UICC were included in the study. Patients followed standard of care. Whole blood gene expression profiling (WBGP) was performed on the day prior to surgery and 1, and 10-14 days after surgery. Samples were collected in Paxgene tubes and labeled cDNA was fragmented and hybridized to Affymetrix GeneChip™ 2.0. Results were corrected for multiple hypothesis testing using the false discovery rate. Pathway analysis was performed through the Molecular Signature Database. Paired fold changes of gene expression were calculated for post-operative compared to pre-operative samples.

*Results*

WBGP of 33,804 genes in 28 patients showed more than 6000 significantly differentially expressed genes between samples from the day prior to surgery and the day after surgery. Pathway gene enrichment analysis showed a downregulation of immunologically relevant pathways. There was a significant downregulation of genes involved in T-cell receptor signaling, antigen presentation, and NK-cell activity after surgery. Furthermore, there was an upregulation of cytokines related to metastatic ability and growth.

*Conclusion*

Whole blood gene expression profiling revealed dysregulation of genes involved in immune surveillance, inflammation, and carcinogenesis after curatively intended laparoscopic colon cancer surgery.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#93 Differential diagnostic impact of DNA methylation profiling on brain tumor classification****Presenting author**

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**Abstract***Introduction*

New diagnostic tools are required for more precise brain tumor diagnostics. Some brain tumor diagnoses are defined by imprecise diagnostic histological criteria leading to interobserver variation. DNA methylation profiling is a new promising approach for improved brain tumor classification. The diagnostic potential of this approach has recently been successfully explored by the German Cancer Research Center. We report the diagnostic impact of a DNA methylation-based classifier tool tested in a clinico-pathological setting.

*Materials and methods*

We prospectively collected tissue from 136 brain tumor cases, where the initial diagnostic workup had led to unclarified diagnoses. DNA methylation profiling was performed using the EPIC BeadChip and IDAT files were generated for data analysis. Data were uploaded to a DNA methylation-based classifier tool and matched to a brain tumor reference cohort with more than 2800 CNS tumors covering more than 80 tumor methylation classes. Reports were generated including a classifier score and a DNA copy-number variation (CNV) profile.

*Results*

In total 90 tumors (66%) appeared to significantly match a methylation class. The initial histopathological diagnoses were changed in 24 out of 90 cases representing a reclassification rate of 27%. This was based on significant methylation profiling scores representing a match to a specific DNA methylation class as well as CNV changes, IHC findings and next-generation sequencing results. A change in tumor grade among the reclassified tumors was observed in 58 % of the tumors, with downgrading of 16 % and upgrading of 42%.

*Conclusions*

DNA methylation profiling is a valuable diagnostic tool for brain tumor classification, especially in cases, where morphological and genetic features are inconclusive. DNA methylation profiling initiated re-evaluation and incorporation of additional tools in the differential diagnostic work up leading to an integrated, precise brain tumor diagnosis.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#94 Signal intensity change on T2 weighted imaging due to PpIX accumulation as possible marker for high grade gliomas****Presenting author**

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**Abstract***Introduction*

Brain cancer continues to be the cancer with the most years of life lost, especially grade IV glioma. Current treatment includes maximal tumor resection followed by concomitant radiation and chemotherapy. Histopathological diagnosis is essential to proceed with medical treatment. A non-invasive diagnostic method is therefore needed for patients unable to undergo surgery and, in the future, for research into possible effects of neoadjuvant chemotherapy.

We hypothesized that the uptake of 5-Aminolevulinic acid (5-ALA) in glioma cells can be measured as a relative change in signal intensity on T2 weighted imaging (T2WI).

*Material and methods*

In patients intended for resection of recurrent high grade glioma, known to have responded to 5-ALA, we compared the mean signal intensity ratio of tumor tissue compared to contralateral white matter on T2WI before and three hours after ingestion of 5-ALA.

T2WI was compared with contrast enhanced T1WI to identify tumor tissue. 20mm<sup>2</sup> regions of interest (ROI) was applied on five MRI slices per patient. 3 ROIs from tumor tissue was compared with three ROIs from contralateral, healthy white matter. 2 ROIs from ipsilateral oedematous tissue was also measured.

Susceptibility weighted imaging was used to avoid haemorrhage and blood vessels

*Results*

Three patients, two males and one female, were included from July to December 2017.

Signal intensity from pre- (1.95 +/- 0.06) and post-5-ALA ingestion (2.05 +/- 0.06) was significantly different with at 95% CI (p<0.001). Oedematous tissue signal intensity pre- (2.02 +/- 0.06) and post (2.04 +/- 0.05) was not significantly different (p=0.25).

*Conclusion*

Preliminary studies show that there is a significant difference in signal intensity due to 5-ALA uptake in high grade gliomas measurable on T2WI MRI. However, more patients are needed to increase statistical certainty.

Currently, inclusion of further patients is being arranged in collaboration with international partners.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#95 Simple biparametric MRI in detection and ruling out significant prostate cancer in biopsy-naïve men – The Biparametric MRI for detection of prostate cancer (BIDOC) study****Presenting author**

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**Abstract***Introduction*

Standard transrectal ultrasound-guided biopsies (SBx) offered to all men with clinical suspicion of prostate cancer (PCa) have limited diagnostic accuracy. Prostate multiparametric MRI seems to improve detection and risk stratification of significant PCa (sPCa), but is time-consuming (~40 min) and cost full. We prospectively assessed the diagnostic accuracy and negative predictive value (NPV) of a more rapid and simple (~15 min) biparametric MRI (bpMRI) method in biopsy-naïve men in detection and ruling out sPCa.

*Materials & methods*

Biopsy-naïve men with clinical suspicion of PCa (elevated PSA level and/or suspicious digital rectal examination) were included and underwent bpMRI (T2-weighted and diffusion-weighted imaging) followed by SBx (all men) and bpMRI targeted biopsies (TBx) in men with suspicious bpMRIs. BpMRI suspicion grades were associated with biopsy results in detection and ruling out sPCa (Gleason score  $\geq 4+3$  or biopsy-core  $>50\%$  of Gleason score  $3+4$ ). We compared the diagnostic performance of SBx in all men (current standard) vs SBx plus TBx (combined biopsies) restricted to men with suspicious bpMRIs. Reference standard were combined biopsies from all men.

*Results*

$N=1,020$  men (median age 67 yrs [IQR 61-71] and median PSA 8.0 ng/ml [IQR 5.7-13.0]) were prospectively enrolled. Any PCa and sPCa was detected in 655/1,020 (64%) and 404/1,020 (40%) men, respectively. Restricting biopsies to men with suspicious bpMRIs meant: 30% (715 vs 1,020 men) could avoid prostate biopsies, improved sPCa diagnoses by 11% (396 vs 351 men), and reduced insignificant PCa diagnoses by 40% (173 vs 288 men)(all  $p<0.001$ ) compared with SBx alone in all men. The NPV of a low-suspicion bpMRI in ruling out sPCa was 97% [CI 97-99%].

*Conclusion*

A low-suspicion bpMRI has a high NPV in ruling out sPCa in biopsy-naïve men and may be used as a triage test before biopsies to improve risk stratification, exclude aggressive disease, and avoid biopsies with its inherent risks.



**Biomarkers and diagnostics + Basic and translational research****Abstract title****#96 Hybrid imaging with PET/MR in oncology****Presenting author**

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**Abstract**

Hybrid imaging by combining either Single Photon Emission Tomography (SPECT) or Positron Emission Tomography (PET) with X-ray Computed Tomography (CT) was introduced for clinical use about 20 years ago. The hybrid combination of PET and CT yielded a strong combination of morphological and non-invasive physiological imaging and proved clinically extremely valuable in especially oncology for cancer diagnosis and staging. Accordingly, PET examinations are predominantly performed as hybrid scans using both PET and CT examinations to gain complimentary information.

Approximately 10 years ago a new hybrid modality became commercially available. With detector technology improvements to PET detectors it became possible to perform magnetic resonance imaging (MR) and PET in a true simultaneous fashion. With the introduction of MRI instead of CT gives new possibilities due to the superior soft-tissue contrast. MRI is also not only an anatomical imaging modality but also a functional imaging modality which can provide additional diagnostic information to value of oncological patients in need of specialized treatment plans or monitoring of treatment response.

The Department of Nuclear Medicine and Clinical Physiology, Odense University Hospital has recently purchased and installed a latest generation PET/MR scanner with the addition of a state of the art 3.0T GE Signa PET/MR hybrid scanner with TOF capabilities.

The experiences in Odense with the new hybrid modality so far regarding both validation of the imaging modality and early experiences with cancer diagnosis in neurology, head and neck and prostate cancer will be presented along with future application of PET/MR in an oncological setting.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#97 Er fornyet billeddiagnostik nødvendig efter neoadjuverende behandling ved rektumcancer?****Presenting author**

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**Abstract***Introduktion*

Som led i udredning af patienter med rektumcancer foretages CT scanning af thorax og abdomen mhp. påvisning af evt. fjerne metastaser samt MR scanning af bækkenet mhp. tumorstaging. Behandlingsstrategi fastlægges på MDT konference. For patienter, som har fået neoadjuverende behandling, gentages den billeddiagnostiske evaluering 6 uger efter endt behandling jf. DCCG retningslinjer, og den endelige behandlingsstrategi fastlægges på en ny MDT konference. Formålet med studiet er at undersøge om fornyet billeddiagnostik efter endt neoadjuverende behandling ændrer den initiale behandlingsstrategi.

*Metode*

Patienter diagnosticeret med primær rektumcancer i perioden 1/1-14 til 31/12-14 på afdelingerne Aarhus, Herning, Bispebjerg, OUH og Roskilde blev identificeret i DCCG.dk's database. Patienter, der modtog neoadjuverende (kemo)-stråle-terapi, er inkluderet i dette studie. Data om behandlingsstrategi besluttet ved MDT konference før og efter neoadjuverende behandling samt fund ved fornyet billeddiagnostik blev indsamlet ved manuel journalgennemgang lokalt på afdelingerne. Data blev registreret online i data capture systemet RedCap.

*Resultater*

I alt 180 patienter indgik i studiet. Hos 13%(n=24) af disse blev behandlingsstrategien ændret efter gennemgang ved MDT konference efter endt neoadjuverende behandling. Årsagen til ændret behandlingsstrategi ved disse var udvikling af fjerne metastaser hos 29,2%(n=7), progression af primær tumor hos 20,8%(n=5), regression af primær tumor hos 25%(n=6) og anden årsag hos 25% (n=6). Af de 7 patienter med fjerne metastaser blev 4 henvist til udelukkende pallierende kemobehandling, 1 aflastet med stent, 2 gennemgik intenderet kurativ behandling af primærtumor og hhv. levermetastase og lungemetastase.

*Konklusion*

Fornyte billeddiagnostik efter endt neoadjuverende behandling ved rektumcancer bør foretages, da der sker sygdomsprogression og -regression hos hver 6. patient, som nødvendiggør ændret behandlingsstrategi.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#98 Predictive biomarkers for malignant pleural mesothelioma****Presenting author**

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**Abstract***Introduction*

Malignant Pleural Mesothelioma (MPM) is an asbestos-related, aggressive malignancy with a median survival of 12 months. Approximately 40% of the MPM patients respond to standard chemotherapy, but there are no predictive biomarkers and the exact mechanisms behind response and resistance are not known. The primary endpoint of the study is to investigate the association of primary and acquired chemotherapy resistance with treatment failure in MPM.

*Materials and methods*

A prospective study of 30 MPM patients from Aalborg University hospital is planned in collaboration with Aalborg University Hospital, Norwegian University of Science and Technology, and Rigshospital. All patients are adults with a verified MPM but no other cancer diagnosis. Blood samples and pleura biopsies are gathered at the time of diagnosis. Patients are being followed up until time of surgery or time of disease progression, where new blood and pleura samples are obtained, if possible. Tumor tissue and blood samples before and after chemotherapy will be analyzed for non-coding RNAs (miRNA, lncRNA), mRNA and DNA methylation profiling. Bioinformatic analyses will be performed. Selected candidate markers will be validated in a retrospective biobank of 450 MPM biopsies.

*Results*

Currently, 23 patients with MPM have been included in the study. The molecular profiling is planned to start in 2019.

*Conclusions*

The identification of candidate single molecules and/or signatures and with a predictive and prognostic value in tumor and in serum for chemo- and immunotherapy will hopefully contribute to more personalized and more effective MPM treatment and thus, reduce excessive treatment and unnecessary costs.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#99 Nye biomarkører for behandling med immun checkpoint inhibitorer ved avanceret ikke-småcellet lungekræft****Presenting author**

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**Abstract***Introduktion*

I Danmark er lungekræft den anden mest almindelige kræftdiagnose, og prognosen er dårlig. Størstedelen af patienterne har ikke-småcellet lungekræft (NSCLC). Siden introduktionen af targeteret behandling, er behandlingsparadigmet skiftet fra en "one-fits-all" strategi med kemoterapi til personlig medicin. Behandling med immun checkpoint inhibitorer (ICI) har i kliniske studier vist bedre overlevelse sammenlignet med kemoterapi. PD-L1 anvendes som biomarkør for behandling med ICI, men er en dårlig prædiktiv markør for behandlingsrespons. PD-L1 kan ændre sig med sygdomsstadie, infektion, inflammation og tidligere antineoplastisk behandling. Der udføres derfor omfattende forskning internationalt i lungecancer og behandling med ICI. Ændringer i behandlingsalgoritme beror på nye biomarkører og nye komplementære metoder. Siden Koordineringsrådet for Ibrugtagning af Sygehusmedicin godkendte Nivolumab, er ICI blevet en del af standard behandlingsalgoritmen for lungecancer.

*Metode*

Et retrospektivt studie på ca. 200 ICI-behandlede patienter med avanceret NSCLC.

Et prospektivt ikke-randomiseret translationelt og hypotesegenererende studie. Ca. 100 patienter med avanceret NSCLC, som er kandidater til behandling med ICI inkluderes konsekutivt. Inkluderede patienter får foretaget rebiopsi ved progression under behandling med ICI eller efter 1 år fra behandlingsstart og fortsat progressionsfrihed. Der tages liquid biopsies ved hvert besøg.

Vævsprøverne analyseres med gensekventering ved Next Generation Sequencing (NGS) og genekspressionsanalyse med et NanoString PanCancer IO360 panel.

*Forventede resultater/konklusion*

Real-life data på patienter med avanceret NSCLC behandlet med ICI.

Vævsprøverne analyseres med henblik på at identificere resistens- og/eller responssignaturer ved behandling af avanceret NSCLC med ICI. Analyse af biomarkører i liquid biopsies kan være et supplement til vævsprøver og afsløre eventuel tumor heterogenitet.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#100 Core needle biopsies of renal masses; prevention of overtreatment with low complications rate****Presenting author**

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**Abstract***Background*

Due to the high incidence of benign lesions in small renal masses  $\leq 4$  cm (SRM), renal tumor biopsies (RTB) are often recommended. Here we describe complications after RTB and evaluate the diagnostic accuracy in SRM.

*Materials and Methods*

Data from patients who underwent percutaneous ultrasound-guided RTB between February 2013 and October 2016 due to CT verified solid renal masses were prospectively collected. Complications were registered and histology from surgical specimens was used to evaluate the accuracy of RTB.

*Results*

Data from 224 consecutive patients were retrieved. Sixteen patients underwent unilateral repeat biopsies or bilateral biopsies; thus, a total of 240 procedures were analyzed. Five patients (2.1%) experienced post-biopsy complications (iatrogenic pneumothorax [n=1], spontaneously resolving hematuria [n=1], and fever [n=3]). There was no correlation between the number of biopsies and occurrence of complications. Overall, 129 had SRM. Biopsies revealed malignancy in 77 (59.7%), and benign histology in 35 (27.1%) whereas 17 (13.2%) were inconclusive. Fifty-six patients with malignant histology and two patients with benign histology underwent surgery. In all cases, the biopsy diagnosis was confirmed upon final histopathology. Of the inconclusive cases, three opted for surgery with benign oncocytoma [n=2] and renal cell carcinoma [n=1]. Overall, RTB led to changes in treatment strategy in 45 patients (34.8%) due to either benign findings or discovery of non-renal cell cancers.

*Conclusion*

RTB have a low complication rate and show excellent accuracy in SRM. RTB can be performed as an outpatient procedure and may serve to prevent overtreatment of benign tumors.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#101 TOX expression in patients with Mycosis fungoides – a potential diagnostic marker?****Presenting author**

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**Abstract***Introduction*

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma and characterized by clonal expansion of atypical T lymphocytes initially affecting the skin. The diagnosis of MF is both a clinical and histological challenge because of the morphological and histological similarities to benign inflammatory dermatitis (BID). It is typically an indolent disorder; however, one third of the patients progress with ulcerating tumors with possible further dissemination to the lymphoid system, blood, and internal organs. Currently, there is no curative treatment for MF and there is an urgent need for the identification of biomarkers that can aid in new diagnostic, prognostic and therapeutic tools. The TOX gene plays an important role in regulating T-cell development and has been proposed to be a potentially diagnostic marker for MF.

*Materials and methods*

Formalin-fixed paraffin-embedded skin biopsies from 43 patients with MF (patch/plaque stage, n = 49 and tumor stage, n = 12) was collected from the archives of the Department of Surgical Pathology, Region Zealand in the period from 1990 to 2016. Skin biopsies from patients with chronic dermatitis were used as controls. TOX mRNA and protein expression were analyzed with the NanoString nCounter technology and immunohistochemistry.

*Results*

TOX mRNA and protein expression were significantly elevated in the early MF group compared to the BID group with a 2.9 and a 2.7 fold increase, ( $p < 0.0001$ ) respectively. The H-score of early MF revealed a 2.5 fold increase ( $p < 0.0001$ ) compared to the BID group. Furthermore, TOX mRNA was increased with the progression from patch/plaque to tumor stage ( $p = 0.002$ ).

*Conclusions*

In the present study, TOX was overexpressed in early MF compared to BID and was increased with the progression from patch/plaque to tumor stage. These findings may indicate that TOX expression could be an additional diagnostic marker for MF.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#102 Characterization and radiosensitivity of HPV-related oropharyngeal squamous cell carcinoma patient-derived xenografts****Presenting author**

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**Abstract***Introduction*

Oropharyngeal squamous cell carcinoma (OPSCC) is the most common head and neck cancer, and is caused by Human papillomavirus (HPV) and smoking.

Purpose of this study was to create a number of patient-derived xenografts (PDXs), compare the models with the corresponding human original tumors, and assess radiosensitivity.

*Materials and methods*

Fresh tumor biopsies from patients with primary, untreated OPSCC were implanted in immunodeficient mice, producing generations of PDX tumors with identical origin.

PDX tumors and their corresponding human original were compared using histology, immunohistochemistry, gene expression profiling and cancer gene targeted sequencing.

Radiosensitivity was evaluated in a growth delay assay (4 – 8 Gy, single fraction).

*Results*

Tumor specimens from 34 OPSCC patients were xenografted, resulting in 12 PDX models that retained histological and immunohistochemical features.

PDX tumors had more genetic variants than the original tumor ( $p < 0.02$ ). There was a high concordance between PDXs and original tumors, with putative driver mutations in TP53, PIK3CA, KMT2D, KMT2C and NOTCH1 retained in the PDX models.

There was high concordance between PDX and original tumors with regard to expression of HPV oncogenes E6 and E7. PDX tumors had higher expression of hypoxia-related genes and lower expression of genes related to inflammation and immune response.

Radiosensitivity studies revealed that the most radiosensitive PDX models were HPV-positive, although one HPV-positive PDX model was relatively radioresistant.

*Conclusion*

PDX models from OPSCC retain histological and immunohistochemical features, as well as important driver gene alterations.

Overall, the PDX model is a promising high-fidelity research tool that may aid in development of personalized medicine. Perspectives include biomarker development, testing of targeted therapies and improvement of radiotherapy.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#103 Differential activity of glucocorticoids and anti-TNF on tumor-specific immune responses****Presenting author**

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**Abstract***Background*

Up to 60% of patients treated with cancer immunotherapy develop severe or life threatening immune-related adverse events (irAEs). Immunosuppression with high doses of glucocorticoids, or anti-TNF in refractory cases, are the mainstay of treatment for CTC grade $\geq$ 3 irAEs. It is currently unknown what is the impact of glucocorticoids and anti-TNF on the activity of the immune system in the tumor microenvironment i.e. whether early use of these agents may jeopardize the antitumor efficacy of cancer immunotherapy.

*Methods*

The influence of clinically relevant doses of dexamethasone (glucocorticoid) and infliximab (anti-TNF) on the activation and killing capacity on tumor-infiltrating lymphocytes (TIL) was evaluated in co-culture assays of TILs and autologous melanoma cells.

*Results*

Dexamethasone, even at low doses (0.01  $\mu$ M), reduced the activation of tumor specific TILs and tumor-killing by 50%. In contrast, the influence of infliximab (10  $\mu$ M) both on T cell activation and on tumor killing was negligible in a majority of cases.

*Conclusions*

Clinically-relevant doses of infliximab do not influence the activity of tumor-specific TILs in vitro, while even low doses of glucocorticoids impair the antitumor activity of TILs. These data support early use of anti-TNF for the treatment of irAEs.



**Biomarkers and diagnostics + Basic and translational research****Abstract title****#104 Extended duration with mediators of acute inflammation functionally impair lymphocytes activated with dendritic cells****Presenting author**

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**Abstract**

Long-term exposure to mediators of acute inflammation might signify a transition into chronic inflammation and could be detrimental in the context of tumor-specific adaptive immunity.

A simple assay was developed based on one-way mixed lymphocyte reaction (MLR), where monocyte-derived dendritic cells (DCs) were co-cultured with allogeneic T cells present in peripheral blood mononuclear cells from healthy volunteers. After five days, an ELISA was performed to quantify the IFN $\gamma$  release as a measure of alloantigen-specific cell activation. Multi-color flow cytometry was performed on DCs and expanded lymphocytes. Maturation with LPS and IFN $\gamma$  were induced one (18 hours), two, three or four days and compared with immature DCs and DCs matured 18 hours with the inflammatory mediators TNF $\alpha$ , IL-1 $\beta$ , IL-6, PGE2 representing chronic inflammation.

Strikingly, levels of IFN $\gamma$  from the MLR reaction decreased on average 29%, 53% and 92% by extending maturation with mediators of acute inflammation (LPS, IFN $\gamma$ ) from one to two, three or four days, respectively (N=3 and quadruplicates). A similar, yet dose-dependent pattern was obtained after titrating down number of DCs added to the MLR reaction (ratio was 1:10; 1:20; 1:40 DCs per PBMCs). DCs matured in four days with LPS and IFN $\gamma$  were the only group with a significant drop in number of viable DCs and their induced levels of IFN $\gamma$  in MLR dropped to the level reached with immature or chronically matured DCs. Surface expression of IL-15R $\alpha$  and CD80 on LPS + IFN $\gamma$ -matured DCs peaked after three days whereas PD-L1, PD-L2, IL-2R $\alpha$  and CD83 further increased after four days of maturation. PD-1+ LAG3+ lymphoblastic T cells peaked in fraction of total T cells when DCs were matured for three days. Thus, phenotype of DCs and T cells do not seem to correlate with levels of IFN $\gamma$ .

Collectively, these results indicate that extended duration of DCs with mediators of acute inflammation functionally impair lymphocytes of relevance in tumor immunology.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#105 The effect of anti-CTLA-4 blockade on the expansion of tumor-infiltrating lymphocytes for adoptive cell therapy in metastatic ovarian cancer****Presenting author**

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**Abstract***Introduction*

The use of in vitro expanded tumor-infiltrating lymphocytes (TILs) in adoptive cell therapy (ACT) has been shown to induce complete and durable tumor regression in patients with advanced melanoma. Efforts are currently underway to expand this treatment modality to other cancer types. The accumulation of TILs in ovarian cancer is prognostic for increased survival while increases in immunosuppressive regulatory T cells are associated with poor outcomes. Within the tumor microenvironment, regulatory cells and expression of co-inhibitory immune checkpoint molecules can lead to the inactivation of TILs. Anti-CTLA-4 therapies can mediate antibody-dependent cell-mediated cytotoxicity and CTLA-4 is expressed on the surface of tumor-infiltrating regulatory T cells. Thus, approaches that directly manipulate co-stimulatory pathways within the initial tumor fragment cultures might improve the expansion of tumor-resident TILs enriched for tumor specificity.

*Materials & Methods*

In this study, we hypothesized that the blockade of the CTLA-4 co-stimulatory pathway in ovarian tumor fragments enhances CD8+ T-cell output and TIL tumor reactivity. Ipilimumab, a CTLA-4-targeting antibody, was added during the initiation of the TIL expansion process and/or during the rapid expansion phase (REP) and the phenotype and functionality were analyzed by flow cytometry.

*Results*

Preliminary data show that blockade of CTLA-4 during the initiation of TIL cultures increased the rate of CD8+ TIL expansion, which is preserved during the REP. Additionally, the tumor reactivity of the TILs expanded from fragments where ipilimumab was added to the culture showed increased tumor reactivity in both young and REPed TILs compared to TILs not cultured with ipilimumab.

*Conclusion*

Our data suggest, that targeting CTLA-4 within the initial tumor fragment favor the expansion of CD8+ TILs and that this manipulation could potentially improve TIL products with respect to phenotype and functionality.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#106 Clinical manufacturing of Chimeric Antigen Receptor (CAR) T cells for adoptive immunotherapy****Presenting author**

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**Abstract***Introduction*

In Europe, cancer is the leading cause of disease related deaths in children. For high risk leukemia patients that develop primary drug resistance and relapse after receiving allogeneic stem cell transplantation, the overall survival rate is less than 25%. Advances in immunotherapy, like chimeric antigen receptors (CARs), has improved treatment options especially for patients with hematological malignancies. Here, patient T cells are genetically modified to express surface antigens and co-stimulatory receptors that maximize tumor recognition and killing. CAR T cell therapy has shown impressive results in relapse acute lymphoblastic leukemia and multiple myeloma with up to 90% sustained remission. Considering this, we aim to establish a foundation for novel research as well as a platform for the production, characterization and the formulation of CAR T-cell products for future clinical trials.

*Material & methods*

The purpose of this study is to design a large-scale manufacturing process enabling the production of clinical doses of genetically engineered T cells in a minimum period of time, initially focusing on CD19+ hematologic malignancies, primarily high risk ALL. Furthermore, we will develop a platform to effectively expand and transiently modify T cells for the preclinical evaluation of next generation CAR T cell therapies.

*Results & conclusion*

We have shown that the production of CAR T cells is feasible using lentiviral vectors and that T-cell product can be rapidly expanded within a few weeks. These antiCD19 cells kill cancer cells in an antigen-specific manner with distinct CD8/CD4 profiles in relation to cytokine secretion

In addition, we show that we can create tumor specific cells through transiently transfected T cells. Thus, this platform will enable us to determine and optimize the safety of novel targets and the therapeutic effectiveness of redirected T cells, and thus accelerate the clinical translation of the safest of new CAR T cells.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#107 In vitro expanded tumor-infiltrating lymphocytes across various sarcoma subtypes highly express LAG3 and comprise multifunctional T cells with tumor killing capacity****Presenting author**

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**Abstract***Introduction*

Tumor-infiltrating lymphocytes (TIL) can be in vitro expanded and have the ability to induce complete and durable tumor regression in some patients following adoptive cell transfer (ACT). In this preclinical study we investigated the feasibility of expanding TILs from sarcomas, as well as performing functional in vitro analyses on these.

*Methods*

Fresh tumor samples from sarcoma patients were obtained, and TILs were isolated and expanded in growth medium containing IL-2. Phenotype and functional analyses were performed using flow cytometry and IFN $\gamma$ -Elispot. Cytotoxicity analyses were performed using Xcelligence.

*Results*

We obtained fresh tumor samples from 28 patients with 8 different sarcoma subtypes, and we were able to expand a minimum of 40 million TIL from 25 of these (90%). Mean expansion times were 32 days (14 - 61) and expanded cells were predominantly CD8<sup>+</sup> T-cells (71 %) of effector memory subtype. T-cells had a mean CD8/CD4 ratio of 0.5 indicating an overrepresentation of CD4<sup>+</sup> TIL. Especially CD8<sup>+</sup> TIL highly expressed LAG3 and to a lesser degree PD-1 and BTLA.

TILs from 10 of 22 tested tumor samples from five different sarcoma subtypes (undifferentiated pleomorphic sarcoma, myxofibrosarcoma, myxoid liposarcoma, myofibroblastic sarcoma and osteosarcoma) demonstrated reactivity against autologous tumor cells using IFN $\gamma$ -Elispot. These results were verified in an intracellular cytokine release assay using flow cytometry and showed multifunctional capacity among the reactive TIL.

*Conclusion*

We were able to expand TIL from 90 % of the acquired tumor samples to numbers needed for possible future clinical ACT implementation. Expanded TILs were a mix of CD4<sup>+</sup> and CD8<sup>+</sup> with CD4<sup>+</sup> being predominant. CD8<sup>+</sup> TIL highly expressed LAG3 and to a lesser degree PD-1 and BTLA. Approximately half of the TIL cultures showed some degree of in vitro tumor reactivity as determined by Elispot and flow cytometry.

**Biomarkers and diagnostics + Basic and translational research****Abstract title****#108 From cold to hot: Increasing tumor immunogenicity by combining checkpoint inhibitors with hyperthermia****Presenting author**

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**Abstract***Introduction*

Despite the success of checkpoint inhibitors (CI) many patients do not respond. Since hyperthermia can influence immune response we have investigated the effect of combining it with a monoclonal antibody (ab) that targets CTLA-4 (anti-CTLA-4 ab) in a non-immunogenic "cold" tumor.

*Methods*

Male CDF1 mice with a 200mm<sup>3</sup> C3H mammary carcinoma in the foot were given either sham treatment (controls); local heat treatment (42.5°C for 1 hour) on day 0; i.p. injection with anti-CTLA-4 ab (10 mg/kg) on day 1, days 1 and 3, or days 1-4; or a combination of heat treatment with anti-CTLA-4 ab. Tumor size was measured daily, and time to reach five times treatment volume (TGT5) recorded. Results are listed as mean ( $\pm$  SE). One-way ANOVA comparison of group means was performed, and a  $P < 0.05$  was considered significant.

*Results*

The TGT5 for the control group was 6.6 days (+ 0.2). For the groups treated with anti-CTLA4 ab on day 1, days 1 and 3, or days 1-4, the TGT5 was 5.8 days (+ 0.4), 5.8 days (+ 0.4) and 6.8 days (+0.3). There were no significant differences between treated animals and controls. In the heat group, the TGT5 was significantly increased to 11.1 days (+ 0.9). This was further increased when heat was combined with anti-CTLA-4 ab to 11.6 days (+ 1.2) for treatment on day 1, 12.9 days (+ 2.7) for days 1 and 3, and 15.4 days (+ 0.8) for days 1-4. Only the group with heat and anti-CTLA-4 ab days 1-4 was significantly increased compared to heat alone ( $p=0.004$ ). One mouse remained without signs of recurrence after 3 months.

*Conclusion*

The C3H mammary carcinoma is insensitive to treatment with CI, and is to be considered as a non-immunogenic "cold" tumor. However, when treated with heat, it becomes "hot"; gets CI sensitive to anti-CTLA-4 ab given on days 1-4. Our data thus clearly show the potential benefit of combining hyperthermia and specific CI to improve tumor immunogenicity. We are currently investigating tumor infiltration of T cells based on histology.

**Clinical epidemiology + Database  
research:  
Poster #109-134**

**Clinical epidemiology + Database research - #109****Abstract title****#109 Danish health register-based research on cancer impact in Denmark (CEDAR Study): An observational, nationwide cohort study****Presenting author**

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**Abstract***Introduction*

In 2015, some 41,000 patients were diagnosed with cancer in Denmark, and more than 280,000 Danes were living with a cancer diagnosis. As patients live longer with their cancer, needs are increasing for diagnostics, treatment, and support to long-term survivors with cancer.

Using the Danish Cancer Registry as the primary ascertainment source and by linkage to other Danish national health registers, Odense Patient data Explorative Network (OPEN) has created a unique resource (CanEpid) for cancer research. This data platform is utilized for the CEDAR Study (Cancer Impact in Denmark) with the aim to characterize cancer subpopulations and the impact of cancer.

*Material and methods*

The CEDAR study is an observational, nationwide study including all patients living with cancer of the lung, breast, bladder, ovary, and prostate as of 31st December 2005 and all patients first-time diagnosed from then up to 31st December 2015. All patients are followed from date of first diagnosis until death or end of 2016. Analyses include epidemiology, morphology, utilization of healthcare resources, treatment patterns, and clinical outcomes.

*Results*

The first results to be presented from the CEDAR study include epidemiologic profiles for the cancer forms concerned, cost-of-illness estimates and forecasting models with projections of incidence, prevalence, and mortality to year 2030.

*Conclusions*

The CEDAR study represents an internationally unique resource for describing the cancer burden in a longitudinal real life setting. The resource may be further enriched by the linkage with data in clinical cancer databases. The framework of analysis may be implemented as a tool for automated epidemiological monitoring. Studies similar to CEDAR are initiated in Norway and Sweden, providing the basis of comparative studies in the Nordic countries using standardized protocols and methods of analysis.

**Clinical epidemiology + Database research****Abstract title****#110 The effect of postoperative gemcitabine on overall survival in an unselected national Danish cohort of patients with pancreatic cancer treated with curative resection****Presenting author**

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**Abstract***Introduction*

In Denmark, each year approximately 150 patients with pancreatic cancer (PC) undergo curative resection. They are offered adjuvant chemotherapy (gemcitabine) as standard. However, the advantage of this treatment on median overall survival (mOS) in daily clinical practice, with patients being older and with more comorbidity is less clear. Therefore, we examined the effect of postoperative gemcitabine on mOS in an unselected national cohort of patients with PC in Denmark.

*Material and methods*

All patients with a curative PC resection in Denmark between 2011 and 2016 were identified in the Danish Pancreatic Cancer Database (DPCD). Data regarding age, comorbidity, stage, type of surgical interventions, chemotherapy and clinical follow up were retrieved. In the study period, 731 patients with ductal adenocarcinoma of the pancreas were treated with a curative PC resection. In all 108 patients were excluded, 30 patients died within 10 weeks postoperatively, 29 patients were treated with other regimens than gemcitabine and 49 patients were treated with neoadjuvant chemotherapy. The 623 patients included, were divided into two groups, receiving postoperative gemcitabine within 10 weeks after resection (CT) or not (NCT).

*Results*

The CT group accounted for 409 (66%) patients and the NCT group for 214. The CT group showed a mOS of 24 months (95% CI; 21-27). No significant difference in survival was observed when compared with the NCT group, who showed a mOS of 22 months (95% CI; 16-26),  $p=0.27$ . For the subgroup of patients with lymph node metastases, a significantly better survival for the CT group were observed with an increased mOS from 14 to 20 months ( $p=0.01$ ).

*Conclusion*

In the national Danish PC cohort undergoing curative resection between 2011 and 2016, no mOS advantage was demonstrated in the patients receiving postoperative gemcitabine. However, there was an increased mOS for the subgroup of patients with lymph node metastases receiving gemcitabine.



**Clinical epidemiology + Database research****Abstract title****#111 Acute pancreatitis and pancreatic cancer risk: A nationwide matched-cohort study in Denmark****Presenting author**

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**Abstract***Introduction*

Acute pancreatitis may be a risk factor for pancreatic cancer. However, findings from studies on this association are conflicting. We investigated the association between acute pancreatitis and increased risk of pancreatic cancer.

*Materials & methods*

We conducted a nationwide, population-based, matched cohort study of all patients admitted to a hospital in Denmark with a diagnosis of acute pancreatitis from January 1, 1980 through October 31, 2012. As many as 5 individuals from the general population without acute pancreatitis were matched for age and sex to each patient with acute pancreatitis. Pancreatic cancer risk was expressed as hazard ratios (HRs) with 95% CIs, calculated using the Cox proportional hazards model. Cox models were stratified by age, sex, and year of pancreatitis diagnosis and adjusted for alcohol- and smoking-related conditions, and Charlson Comorbidity Index score.

*Results*

We included 41,669 patients diagnosed with incident acute pancreatitis and 208,340 comparison individuals. Patients with acute pancreatitis had an increased risk of pancreatic cancer compared with the age- and sex-matched general population throughout the follow-up period. The risk decreased over time but remained high after more than 5 years of follow up (adjusted HR, 2.02; 95% CI, 1.57-2.61). Two- and 5-year absolute risks of pancreatic cancer among patients with acute pancreatitis were 0.68% (95% CI, 0.61%-0.77%) and 0.85% (95% CI, 0.76%-0.94), respectively.

*Conclusions*

In a nationwide, population-based, matched cohort study, we observed an association between diagnosis of acute pancreatitis and long-term risk of pancreatic cancer.

**Clinical epidemiology + Database research****Abstract title****#112 The association between use of the photosensitizing drug hydrochlorothiazide, and risk of skin cancer****Presenting author**

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**Abstract***Introduction*

Hydrochlorothiazide, one of the most frequently used diuretic and antihypertensive drugs in the United States and Western Europe, is photosensitizing and has previously been linked to lip cancer.

*Materials and methods*

In five separate case-control studies, we studied the association between use of HCTZ and risk of non-melanoma skin cancer (NMSC), melanoma, Merkel cell carcinoma and malignant adnexal skin tumours (MAST). Cases were identified via the Danish Cancer Registry and matched to population controls. Using conditional logistic regression, adjusting for predefined potential confounders, we calculated odds ratios (ORs) for basal cell carcinoma, squamous cell carcinoma, melanoma, Merkel cell carcinoma and MAST associated with HCTZ use. We also examined dose-response effects and associations with the use of drugs with similar indications as HCTZ.

*Results*

We observed a steep dose-response pattern for squamous cell carcinoma, with ORs reaching 7.38 (6.32-8.60) with use of  $\geq 200\ 000$  mg HCTZ. A weak dose-dependent association was seen for basal cell carcinoma, with an OR of 1.54 (1.38-1.71) associated with use of  $\geq 200\ 000$  mg HCTZ. For melanoma, we found a weak association 1.22 (1.09-1.36) with HCTZ use ( $\geq 50\ 000$ mg), driven by ORs for nodular 2.05 (1.54-2.72) and lentigo melanoma 1.61 (1.03-2.50). The ORs for Merkel cell carcinoma and MAST associated with highest use ( $\geq 100\ 000$ mg) of HCTZ was 3.3 (1.3-8.3) and 5.6 (2.4-13.3), respectively. Besides a known association between use of furosemide and risk of Merkel cell carcinoma (OR; 1.9), analyses for other diuretics and antihypertensives yielded neutral associations for all outcomes.

*Conclusions*

In conclusion, HCTZ use was associated to all included UV-light susceptible skin cancers. We found substantially increased risk of squamous cell carcinoma, and a potential association with lentigo and nodular melanoma. Further there was an association to basal cell carcinoma, Merkel cell carcinoma and MAST.

**Clinical epidemiology + Database research****Abstract title****#113 Use of prescription drugs among ovarian cancer patients in Denmark****Presenting author**

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**Abstract***Introduction*

Ovarian cancer patients often suffer from chronic diseases at diagnosis. Thus, drug use for prophylaxis or treatment of concomitant disease is considerable at diagnosis of ovarian cancer. We aimed to describe general drug utilization among post-menopausal ovarian cancer patients, with focus on temporal patterns in drug use.

*Materials & Methods*

We identified all post-menopausal women diagnosed with epithelial ovarian cancer in Denmark 2005-2012 and a comparison cohort of age-matched (1:4) women without cancer. We calculated rates of new and total drug use and examined use of the most common new and prevalent drug classes before and after ovarian cancer diagnosis. Drug exposure rates were specified by histological type and clinical stage of ovarian cancer.

*Results*

We identified 2,742 ovarian cancer patients. The rate of new drug treatment began to increase from 3-5 months prior to diagnosis and peaked in the first month after diagnosis with 99 new types of drug therapy per 100 patients. Immediate post-diagnosis drug therapy mainly included antiemetics, proton pump inhibitors, hypnotics, and opioids. Although declining, the rate of new drug use remained substantially higher among ovarian cancer patients than among cancer-free controls throughout the 3-year post-diagnosis follow-up period. The number of prevalent drugs increased slightly from a median of four drugs (interquartile range [IQR] 2-7) prior to diagnosis to five (IQR 2-8) shortly after the diagnosis. The use of prophylactic drugs, e.g., statins, antihypertensives, and low-dose aspirin, decreased only slightly after diagnosis. We found little variation according to histological type, whereas the patterns were slightly more pronounced among women with non-localized disease.

*Conclusions*

Drug use among post-menopausal ovarian cancer patients was substantial and varied markedly in relation to the time of cancer diagnosis, although only limited changes were seen in the use of prophylactic drugs.

**Clinical epidemiology + Database research****Abstract title****#114 Use of antipsychotics and risk of breast cancer: A Danish nationwide case-control study****Presenting author**

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**Abstract***Introduction*

The use of some antipsychotics increases prolactin levels, which might increase the risk of breast cancer. Existing evidence is conflicting and based on sparse data, especially for the increasingly used second-generation antipsychotics. We conducted a nationwide case-control study of the association between antipsychotic use and incident breast cancer.

*Material and Methods*

From the Danish Cancer Registry, we identified women with a first-time diagnosis of breast cancer 2000-2015 (n=60,360). For each case, we age-matched 10 female population controls. Using conditional logistic regression, we calculated odds ratios (ORs) for breast cancer associated with use of antipsychotics. We stratified antipsychotics by first and second generation status and by ability to induce elevation of prolactin.

*Results*

4,951 cases (8.1%) and 47,643 controls (7.1%) had ever used antipsychotics. Long-term use ( $\geq 10,000$  mg olanzapine equivalents) was associated with breast cancer, with an adjusted OR of 1.19 (95%CI, 1.07, 1.33). A weak dose-response pattern was seen, with ORs increasing to 1.27 (95% CI 1.02, 1.60) for  $\geq 50,000$ mg olanzapine equivalents. Associations were similar for first- and second-generation antipsychotics (ORs 1.18 vs 1.12), but also for non-prolactin inducing antipsychotics (OR 1.17). Among second-generation antipsychotics, positive associations were found for prolactin-elevating but not for non-prolactin elevating antipsychotics.

*Conclusions*

Overall, our results do not suggest a clinically important association between antipsychotic use and risk of breast cancer. The importance of drug-induced prolactin elevation is unclear but may be of relevance for second-generation antipsychotics.

**Clinical epidemiology + Database research****Abstract title****#115 DBCG COR: The risk of radiotherapy induced heart disease in women treated for early stage breast cancer****Presenting author**

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**Abstract***Introduction*

Radiotherapy (RT) is essential in the adjuvant treatment of breast cancer reducing the risk of recurrence and improving overall survival. RT may increase the risk of developing a heart disease, and the risk depends on the RT dose to the heart. Due to the anatomical localization of the heart, the ventral part receives a large RT dose.

The aim of this study is to establish a dose-response relationship linking RT dose to the heart and the risk of radiation induced heart disease based on individual characteristics.

*Material and methods*

The study is based on data from the Danish Breast Cancer Group (DBCG), a national database that registers diagnostics, treatment and follow-up in breast cancer patients, and West Danish Heart Database (VDH) that registers all invasive heart procedure in Jutland and Funen. In the DBCG database, 97.137 women have been registered with a diagnosis of breast cancer in the period 1990-2016. Among these women VDH has registered 3.942 procedures, with 28 % registered before the breast cancer diagnosis and 72 % after the breast cancer diagnosis. Since year 2000 the majority of RT treatment plans are based on CT scans, thus the RT dose to the heart can be evaluated based on individual treatment characteristics. These data make it possible to investigate the localization of heart disease in women treated with and without RT. For those treated with RT dose corresponding to the heart disease is estimated. A case-control study will be used to establish a dose-response relationship.

*Conclusion*

The dose-response relationship linking RT dose to the heart and the risk of RT induced heart disease will evaluate the risk of heart disease on an individual basis. The results may contribute to optimal selection of patients to RT, including treatment with protons.

**Clinical epidemiology + Database research****Abstract title****#116 Risk factors of sentinel and non-sentinel lymph node metastases in patients with ductal carcinoma in situ of the breast****Presenting author**

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**Abstract***Introduction*

Ductal carcinoma in situ (DCIS) is a non-invasive breast lesion that does not spread to the lymphatic system. However, unexplained axillary lymph node metastases have been detected in some DCIS patients, possibly because of occult invasion or iatrogenic tumor cell displacement. The significance of these metastases is unknown and brings into question the need for axillary treatment and upstaging.

*Aim*

To identify risk factors of sentinel lymph node (SN) and non-SN metastases, including the risk of iatrogenic tumor cell displacement in connection with a recent excisional biopsy, in patients diagnosed with DCIS.

*Methods*

In this register-based study 1793 Danish women with a final diagnosis of DCIS were enrolled, including 77 women with, and 1716 women without a positive SN (isolated tumour cells (ITC), micro- or macrometastases). The patients were identified in the Danish breast cancer database between 2001 and 2015. The association between age, year, DCIS size, Van Nuys classification, palpability and biopsy method and a positive SN was evaluated.

*Results*

Of the 1793 women with DCIS, 77 (4.3%) had a positive SN; 16 (0.9%) had macrometastases, 45 (2.5%) had micrometastases and 16 (0.9%) had isolated tumor cells (ITC). Six (9.5%) women with a positive SN also had positive non-SNs. In adjusted analysis, a positive SN was associated with younger age, increased size, palpability and surgical excisional biopsy.

*Conclusion*

The overall risk of SN metastases in patients with DCIS on final pathology is low and less than 10% of these patients have non-SN metastases. This argues against using axillary lymph node dissection in this group. The odds of a positive SN after surgical excisional biopsies showed more than a four-fold increase, indicating iatrogenic tumor cell displacement. The use of extensive axillary surgery in these patients and upstaging of patients with iatrogenic displacement of tumor cells to the lymph nodes both need to be reconsidered.

**Clinical epidemiology + Database research****Abstract title****#117 Histopathologic characteristics in synchronous bilateral breast cancer patients: a nationwide Danish cohort study from 1999-2015****Presenting author**

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**Abstract***Background*

The purpose of the present study was to describe the histopathologic characteristics of synchronous bilateral breast cancer (SBBC), and to compare these characteristics with those of unilateral breast cancer (UBC).

*Materials and methods*

Data was retrieved from the Danish Breast Cancer Group (DBCG) database and the Danish Pathology Register. Inclusion criteria for SBBC patients were patients registered in the DBCG database from 1999-2015 with two breast cancers diagnosed within 4 months of each other. Exclusion criteria: only DCIS on one side, previous malignancy, disseminated cancer, locally advanced cancer, and patients who received neoadjuvant therapy. SBBC patients were compared to all UBC patients registered in the DBCG database from 1999-2015, with the same exclusion criteria as SBBC patients. Differences in histopathologic characteristics were explored using logistic and multinomial regression analyses. Correlation between right and left tumor in the same SBBC patient was accounted for using a Generalized Estimating Equation correlation structure. Crude and adjusted models were performed, the latter adjusting for relevant clinical and histopathologic characteristics.

*Results*

A total of 1,215 SBBC and 61,050 UBC patients were included. SBBC patients had a higher proportion of lobular carcinomas (adj. OR, lobular vs ductal: 1.30, 95% CI: 1.14-1.48), and tumors were more often estrogen receptor (ER) positive (adj. OR: 1.90, 95% CI: 1.61-2.23), combined ER positive/HER2 negative, and of lower grade (adj. OR's of 0.77 and 0.42, grade II and III vs I respectively). Tumor size for SBBC patients was larger when comparing UBC patients with the largest tumor in the SBBC patient, but smaller when comparing both tumors with UBC patients, taking account for correlations. No difference was observed in nodal involvement.

*Conclusions*

SBBC patients more often present with lobular carcinomas, and are more often of a less aggressive subtype.

**Clinical epidemiology + Database research****Abstract title****#118 Validering af Dansk Kolorektal Cancer Database – på vegne af Danish Colorectal Cancer Group's (DCCG) Videnskabelige Udvalg****Presenting author**

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**Authors**

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**Abstract***Introduktion*

Danish Colorectal Cancer Group (DCCG.dk) grundlagde i 2001 en landsdækkende database, hvori alle patienter med tyk- og endetarmskræft i Danmark bliver registreret. Der registreres detaljer om diagnosticering, omfang af sygdom, behandling, komplikationer og resultater af behandlingen. Databasen er en klinisk kvalitetsdatabase med en patientkomplethed >99% og siden 2001 er der produceret årsrapporter med fokus på behandlingsresultaterne. Disse rapporter, samt videnskabelige studier baseret på databasens data, har bidraget betydeligt til at forbedre behandlingen af tyk- og endetarmskræft. Databasens vigtighed er således indiskutabel. Dette til trods er datakompletheden kun blevet valideret en enkelt gang, omfattende udvalgte data for 87 patienter fra 2001. Dette projekt har til formål at evaluere DCCG databasens datakomplethed og -kvalitet.

*Materialer & Metoder*

Da det ikke har været muligt at opnå tilladelse til gennemgang af journaler fra hele databasens levetid valideres i første omgang data fra årene 2014-2017. Fra disse år udvælges en stikprøve på 5% sv.t. 1.000 patientforløb, og kernevariable fra databasen genregistreres herefter af specialiserede kolorektalkirurger på de enkelte afdelinger. Data registreres i sikret database online (REDCap). De udvalgte variables komplethed og nøjagtighed vil blive vurderet bl.a. ved udregning af kappa-værdier som proportionen mellem den aktuelle overensstemmelse ud over den tilfældige og den potentielle overensstemmelse ud over den tilfældige.

*Resultater*

I skrivende stund pågår indtastningen af de udvalgte kernevariable. Aktuelt er 390 patientforløb færdigregistrerede. Endelige resultater ventes at kunne præsenteres i løbet af sommeren 2018.

*Konklusioner*

Denne validering forventes at blive af stor betydning for gennemslagskraften af fremtidige forskningsprojekter baseret på databasen, ligesom det er håbet, at projektet kan inspirere andre nationale kliniske kræftdatabaser til gennemgang og validering af data.



**Clinical epidemiology + Database research****Abstract title****#119 Short education, low income, and living alone increase the risk of 1-year mortality after acute colorectal cancer surgery, a nationwide cohort study****Presenting author**

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**Authors**

Thea Helene Degett (TD), Jane Christensen (JC), Linda Aagaard Thomsen (LT), Lene Hjerrild Iversen (LI), Ismail Gögenur (IG) and Susanne Dalton (SD)

**Abstract***Introduction*

Acute colorectal cancer surgery is associated with a high mortality. Risk factors still need to be investigated in order to improve survival after surgery. The aim of this study was to examine the influence of socioeconomic position on the risk of undergoing acute versus elective colorectal cancer surgery. Furthermore, investigate if socioeconomic position has an effect on 1-year mortality once the patients undergo acute colorectal cancer surgery.

*Materials and methods*

All patients registered with a surgical procedure in the Danish Colorectal Cancer (DCCG.dk) database from 2007 to 2015 were included in this study. The effect of socioeconomic position was measured by highest attained education, income, urbanicity and cohabitation status. Outcome data were extracted from Statistics Denmark. Additional information on acute stent insertion and diverting stoma was retracted from the National Patient Register. Logistic regression and cox proportional hazard was used to evaluate the associations in the first and second study question, respectively.

*Results*

35,699 patients underwent surgery, 30,352 (85%) as an elective and 5,317 (15%) as an acute procedure. Short (OR = 1.24, 95% CI: 1.12-1.38) and medium (OR = 1.13, 95% CI: 1.03-1.24) education, and living alone (OR = 1.35, 95% CI: 1.26-1.46) increased the risk of an acute versus an elective procedure. 1-year mortality after acute surgery was 41%. Short education (HR = 1.18, 95% CI: 1.03-1.35), low income (HR = 1.19, 95% CI: 1.03-1.37), and living alone (HR = 1.28, 95% CI: 1.16-1.42) increased the risk of 1-year mortality after acute colorectal cancer.

*Conclusion*

Low socioeconomic position increased the risk of having acute versus elective colorectal cancer surgery. Furthermore, short education, low income and living alone were associated with an increase in 1-year mortality after acute colorectal cancer surgery.

**Clinical epidemiology + Database research****Abstract title****#120 ACE-I/ARBs and risk of acute kidney injury after colorectal cancer surgery: A population-based cohort study****Presenting author**

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**Abstract***Introduction*

Angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin-receptor blockers (ARBs) are commonly used drugs with potential nephrotoxicity. It is unknown whether use of ACE-I/ARBs affects the risk of acute kidney injury (AKI) after colorectal cancer (CRC) surgery. We assessed the impact of use of ACE-I/ARBs on AKI risk after surgery for CRC.

*Methods*

From the Danish Colorectal Cancer Group Database we identified all patients who underwent CRC surgery from 2005-2015 in northern Denmark. Based on reimbursed prescriptions, patients were characterized as current users of ACE-I/ARBs ( $\geq 1$  prescription within 90 days before surgery), former users ( $\geq 1$  prescription in the period 91-365 days before surgery and none within 90 days prior to surgery), or non-users (no prescriptions within 1 year before surgery). 7-day postoperative AKI was ascertained based on changes in plasma creatinine. We computed incidence proportions (risk) of AKI with 95% confidence intervals (CI) for current, former, and non-users of ACE-I/ARBs, including death as a competing risk. Adjusted risk ratios (aRRs) were computed using log-binomial regression controlled for potential confounders. Analyses were stratified by subgroups of ACE-I/ARBs users to address any difference in impact.

*Results*

Our analysis included 9,932 patients, among whom 21.3% were ACE-I/ARB current users, 6.4% were former users, and 72.3% were non-users. The 7-day postoperative risk of AKI for current users was 26.4% (95% CI: 24.6%-28.3%), compared to 25.2% (95% CI: 21.9%-28.6%) for former users, and 17.8% (95% CI: 17.0%-18.7%) for non-users. The aRRs of AKI 1.09 (95% CI: 1.06-1.12) for current users and 1.13 (95% CI: 1.08-1.19) for former users, compared to non-users. The stratified analyses yielded similar estimates across subgroups.

*Conclusion*

Current and former users of ACE-I/ARBs may have increased susceptibility to AKI, requiring special attention to prevent its development following surgery for CRC.

**Clinical epidemiology + Database research****Abstract title****#121 Exposure to phthalate-containing prescription drugs and the risk of colorectal adenocarcinoma: a Danish nationwide case-control study****Presenting author**

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**Authors**

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**Abstract***Background*

Phthalates are suspected endocrine disrupters; however, the carcinogenic potential is still unclear. In vitro studies have demonstrated that phthalates interfere with several cellular mechanisms involved in colorectal cancer development. Pharmaceuticals are a major source of phthalate exposure.

*Objective*

To examine whether there is an association between cumulative pharmaceutical ortho-phthalate exposure and risk of colorectal adenocarcinomas.

*Methods*

We conducted a Danish nationwide case-control study including all patients with incident colorectal adenocarcinoma 2008-2016 (n=19,436). Each case was matched to five controls. Linking information from a database maintained by the Danish Medicines Agency to the Danish Prescription Registry, we quantified cumulative phthalate exposure to ortho-phthalates from orally administered drugs. Further we specified by exposure to the individual ortho-phthalates diethyl phthalate (DEP) and dibutyl phthalate (DBP). The association was estimated using conditional logistic regression.

*Results*

6,777 cases (26%) and 70,771 controls (27%) had been ever-exposed to any ortho-phthalate from drug products presenting an adjusted OR at 0.97 (95%CI, 0.94-1.00) for the risk of colorectal adenocarcinoma. Major exposure (>500 mg) to any ortho-phthalate yielded an adjusted OR at 0.88 (95%CI, 0.81-0.95). No clear dose-response pattern was observed. Associations were similar for the individual phthalates. High DEP exposure (>500 mg) yielded an adjusted OR at 0.88 (95%CI, 0.80-0.96) and high DBP exposure (>500 mg) yielded an adjusted OR at 0.87 (0.73-1.05).

*Conclusion*

In this study, cumulative exposure to more than 500 mg ortho-phthalate as a drug-ingredient was associated with a decreased risk of colorectal adenocarcinoma. Our findings were opposite to our study hypothesis and biological rationale.

**Clinical epidemiology + Database research****Abstract title****#122 Treatment and survival among Danish patients with colorectal synchronous peritoneal metastases****Presenting author**

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**Authors**

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**Abstract***Aim*

To describe treatment and survival among patients with synchronous peritoneal metastases (S-PM) from colorectal cancer (CRC).

*Method*

The study was performed as a population-based study of Danish patients diagnosed with S-PM between 2014-2015 and followed until January 2017 (follow-up in June 2018 is planned). Patients with S-PM were identified using the Danish Colorectal Cancer Group database, the Danish National Patient Registry and the Danish Pathology Registry. The same registries were used to identify treatment characteristics within 180 days after CRC diagnosis. Treatment was categorized into 4 groups based on specific algorithms. Patients were excluded if another cancer was recorded within 5 years prior to CRC diagnosis.

One- and 2-year survival rates were computed using Kaplan-Meier survival analysis for patients who had survived 180 days after CRC diagnosis.

*Results*

Among 468 patients with S-PM, 102 (22%) received 'no treatment', 210 (45%) received 'alleviating surgery and/or systemic chemotherapy', 127 (27%) had a 'colonic/rectal resection of the primary tumour +/- systemic chemotherapy' and 29 (6%) received 'cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC)'. Preliminary estimates show 1- and 2-year crude survival rates of 53% (95 CI:29;72) and 24% (95 CI:8;45) when receiving 'no treatment', 65% (95 CI:57;73) and 24% (95 CI:17;33) when 'alleviated with surgery and/or systemic chemotherapy', 69% (95 CI:59;77) and 36% (95 CI:26;46) after a 'colonic/rectal tumour resection +/- systemic chemotherapy', and 100% (95 CI: NA) and 95% (95 CI:68;99) when treated with 'CRS+HIPEC'.

*Conclusion*

There is a large difference in the treatment of patients with S-PM even though CRS+HIPEC is a well-known treatment option with favourable outcome. One can expect that the population-based survival will increase once CRS+HIPEC is performed in a larger proportion of these patients.

**Clinical epidemiology + Database research****Abstract title****#123 Risk factors for metachronous peritoneal metastases: A nationwide population-based cohort study of Danish colorectal cancer patients****Presenting author**

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**Presenting authors and affiliation**

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**Abstract***Aim*

To identify risk factors for metachronous peritoneal metastases(M-PM) after curative colorectal cancer(CRC) surgery.

*Method*

This nationwide register-based cohort study included all Danish CRC patients from 2006-2015 using the Danish Colorectal Cancer Group database, The Danish Pathology Registry and The Danish National Patient Registry.

Peritoneal metastases(PM) were divided into synchronous PM(S-PM) diagnosed within -/+ 180 days of CRC diagnosis, and M-PM diagnosed  $\geq$  180 days after CRC diagnosis.

Patients were excluded if another cancer was recorded within 5 years prior to CRC diagnosis, and included in the analysis of risk factors for M-PM if they underwent curative treatment for CRC.

Potential predictors of M-PM were estimated by a multivariable risk regression, treating death and other cancer as competing risks. One and 3-year risk differences(RD) are presented as the absolute difference between groups.

*Results*

During 2006-2015, 37,734 patients were included. The prevalence of S-PM increased from 2% in 2006 to 5% in 2015.

In total, 22,582 patients met the inclusion criteria for the analysis of risk factors for M-PM. The 1-year risk of M-PM was 0.9%(95% CI:0.8;1.1) increasing to 3.1%(95% CI: 2.8;3.4) after 9 years.

Following variables were associated with a higher risk of M-PM: Right-sided colonic cancer(1-year: *right colon vs. rectum*, 0.60%(0.22, 0.98) and 3-year: 0.93%(0.34, 1.51)), advanced tumour category(T4- vs. T1-category 1-year: 2.97%(2.19; 3.75) and 3-year: 6.12%(4.98; 7.25)) and lymph node metastasis(N2 vs. N0 1-year: 2.58%(1.87; 3.27) and 3-year: 4.32%(3.29; 5.34)).

A subanalysis revealed that the positive resection margins were associated with an increased risk of M-PM (1-year: *R1 vs. R0*: 4.16%(1.77, 6.54) and 3-year: 6.18%(2.81, 9.55).

*Conclusion*

Patients with right-sided colonic cancer, high T-category, lymph node metastasis, and positive resection margins have a higher risk of developing PM. Therefore, a close follow-up program is recommendable.

**Clinical epidemiology + Database research****Abstract title****#124 Local recurrence rate in a national Danish patient cohort after curative treatment for rectal cancer****Presenting author**

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**Abstract***Introduction*

Several trials have shown that preoperative (chemo)radiotherapy (CRT) reduces local recurrence rates (LRRs) in rectal cancer (RC). The use of CRT varies greatly between countries. It is unknown whether the restrictive use of CRT in Denmark results in a higher LRR relative to other countries. The aim was to evaluate the LRR in a national Danish consecutive cohort of patients with RC.

*Materials & methods*

All data from patients with RC in Denmark in 2009-2010 who were operated on with curative intent were retrieved from the Danish Colorectal Cancer Group database. Patients with metastases at the time of diagnosis, patients with synchronous colon cancer and patients in whom only local surgical procedures were performed were excluded. In total, 1,633 patients met the inclusion criteria. Clinical follow-up was at least five years with a cut-off date of 31 December 2015.

*Results*

Clinical follow-up was 5.4 years (median) with an interquartile range of 4.5-6.1 years.

Of all included patients, 479 (29%) were treated with preoperative long-course CRT. Local recurrence was found in 68 patients, resulting in an LRR of 4.2%, and 182 (11%) patients developed distant metastases. Five-year overall survival was 74% (95% CI: 71.64-75.91).

*Conclusions*

Five-year follow-up of curatively treated patients with RC in Denmark revealed a low LRR. This figure is identical to those reported in other Nordic countries, despite Denmark's considerably stricter guidelines for CRT. The obtained results justify the currently adopted restrictive use of preoperative CRT in Denmark.

**Clinical epidemiology + Database research****Abstract title****#125 Effectiveness of colorectal cancer screening in detecting earlier-stage disease - a nationwide cohort study in Denmark****Presenting author**

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**Authors**

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**Abstract***Introduction*

Most studies of the effectiveness of screening for colorectal cancer (CRC) using fecal occult blood tests (FOBT) are based on the guaiac FOBT. However, the fecal immunochemical test (FIT) is now commonly used in screening. We aimed to evaluate the effectiveness of FIT-based screening for CRC on the number of incident CRC diagnoses and stage at diagnosis for individuals who were invited for screening vs not invited.

*Material and methods*

The study was designed as a register-based retrospective cohort study during the first 16 months of the prevalence round of a FIT-based CRC screening program. A total of 402,826 residents of Denmark (50–72 years old) were randomly invited to undergo CRC screening within the study period and 956,514 were randomized to be invited thereafter. We obtained information on CRC diagnosis, date, and stage at diagnosis from the Danish Colorectal Cancer Group database. Cancer incidence per 100,000 invited/not yet invited individuals was calculated along with the overall and stage-specific relative risk (RR) of CRC among invited compared with not yet invited individuals.

*Results*

CRC incidence during the study period was 339.4/100,000 invited individuals and 169.6/100,000 not yet invited individuals. For invited women compared to not yet invited women, the RR of being diagnosed with stage I CRC was 3.39 (95% CI, 2.61–4.39); with stage II CRC was 2.16 (95% CI, 1.71–2.72); with stage III CRC was 1.37 (95% CI, 1.08–1.75), and with stage IV CRC was 0.92 (95% CI, 0.68–1.23). For invited men compared to not yet invited men, the RR of being diagnosed with stage I CRC was 3.71 (95% CI, 2.97–4.64); with stage II CRC was 2.26 (95% CI: 1.84–2.77), with stage III CRC was 1.88 (95% CI: 1.53–2.30), and with stage IV CRC was 1.20 (95% CI, 0.95–1.52).

*Conclusion*

The findings from this study substantiate the introduction of FIT-based CRC screening in order to detect CRC in earlier stages and thereby secure better prognosis for the patients.

**Clinical epidemiology + Database research****Abstract title****#126 Oversete colorektal cancer tilfælde ved koloskopi i Danmark - betydende faktorer og udvikling over tid****Presenting author**

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**Authors**

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**Abstract***Introduktion*

Kikkertundersøgelse af tyktarmen (koloskopi) er den fortrukne metode til diagnostik af tyktarmskræft (KRC). KRC antages at udvikle sig fra polypper (adenomer) over en længere årrække. Ved koloskopi kan KRC og polypper diagnosticeres, polypperne kan fjernes umiddelbart. Jo tidligere KRC opdages jo bedre prognose. Desværre er ingen undersøgelse perfekt og udenlandske undersøgelser har dokumenteret en høj rate af oversete KRC. Formålet med vores undersøgelse er

- 1)Undersøge andelen af oversete KRC ved koloskopi i Danmark.
- 2)Undersøge hvilke faktorer, der var associeret med overset KRC.

*Metode*

Fra det nationale patientregister identificerede vi alle patienter, der havde fået foretaget mindst én koloskopi i perioden 2001-2012 og fra cancerregisteret identificerede vi alle KRC i perioden 2001-2015. En KRC fundet ved koloskopi blev defineret som en koloskopi med efterfølgende KRC-diagnose indenfor 6 mdr. Én koloskopi med efterfølgende KRC 6-36 mdr efter blev defineret som overset KRC.

Multivariate poisson regressionsanalyse blev anvendt til at identificere faktorer associeret med overset KRC.

*Resultater*

Vi fandt 11.631 patienter med mindst én koloskopi og efterfølgende KRC indenfor 3 år. Heraf havde 1.104 mindst én skopi i perioden 6-36 mdr før KRC diagnose. Antallet af oversete cancer ved koloskopi er således 9,5%.

Poisson regressionsanalyse viste, at (ældre) koloskopi-år, divertikulit, Charlson comorbidity score, højresidig placering af colontumor, colitis ulcerosa, bekræftet/mistænkt arvelig KRC og lille tumorstørrelse er associeret med overset KRC ved koloskopi.

*Konklusion*

Der overses et højt antal af kræfttilfælde ved koloskopi i Danmark, men andelen er faldende over tid. Patienten med betydelig comorbiditet, mistænkt/bekræftet disponering for arvelig KRC, divertikulit eller Colitis Ulcerosa bør koloskoperes af erfaren koloskopør for at mindske risikoen for at overse KRC. Koloskopører bør være ekstra opmærksomme på at gennemse højre side af colon.



**Clinical epidemiology + Database research****Abstract title****#127 Why are estimates of overdiagnosis in routine breast cancer screening so profoundly different?****Presenting author**

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**Abstract***Introduction*

Overdiagnosis estimates have varied substantially from 1% to more than 50%. This has caused confusion. The discussions have been complicated by the fact that population and study design have varied substantially between studies. To help assess the impact of study design choices on the estimates, we compared them on a single population

*Materials and Methods*

A cohort study from Funen County, Denmark, recently suggested little (~1%) overdiagnosis. It followed women invited to screening for up to 14 years after screening had ended. Using publicly available data from Funen, we recreated the designs from five high-estimate, highly cited studies from various countries. Selected studies estimated overdiagnosis to be 25–54%. Their designs were adapted only to the extent that they reflect the start of screening in Funen in 1993.

*Results*

The reanalysis of the Funen data resulted in overdiagnosis estimates that were remarkably similar to those from the original high-estimate age-period studies, 21–55%. In additional analyses, undertaken to elucidate the effect of the individual components of the study designs, overdiagnosis estimates were more than halved after the most likely changes in the background risk were accounted for and decreased additionally when never-screened birth cohorts were excluded from the analysis.

*Conclusions*

The same data give both low and high estimates of overdiagnosis, it all depends on the study design. A common methodological background in observational epidemiology could avoid invalid results, false controversies and confusion in the communication with women. This study showed that overdiagnosis estimates should in the future be requested to adequately control for the background risk and include an informative selection of the studied population to achieve valid and comparable estimates of overdiagnosis.

**Clinical epidemiology + Database research****Abstract title****#128 Cerebralt metastaserende melanom – en opgørelse af patienter med ny-diagnosticeret metastatisk melanom i DK i 2016****Presenting author**

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**Abstract***Baggrund*

Patienter med metastatisk melanom får spredning til hjernen i deres sygdomsforløb. Median overlevelsen var 3 måneder før indførelsen af nye behandlinger. Studier tyder på effekt intrakranielt af de nye behandlinger (BRAF-/MEK hæmmere/checkpoint-hæmmere), specielt hos patienter med asymptomatiske cerebrale metastaser.

*Formål*

At undersøge en dansk kohorte af patienter med nydiagnosticeret metastaserende melanom fra 2016 med henblik på tidspunkt for diagnosticering af cerebrale metastaser, symptomgivende vs asymptomatiske cerebrale metastaser, behandling og overlevelse (overall survival (OS)).

*Metode*

Fra Dansk Metastatisk Melanom Database blev en kohorte af nydiagnosticerede patienter med stadie IV sygdom henvist til Kræftafdelingen, Aarhus Universitetshospital og Onkologisk afdeling, Herlev Hospital udvalgt. Det svarer til 75 % af den samlede danske kohorte af patienter med nydiagnosticeret metastaserende melanom henvist i 2016.

*Resultater*

Ud af 251 nyhenviste patienter i 2016 havde eller fik 98 patienter cerebrale metastaser under behandlingsforløbet. 58 patienter havde cerebrale metastaser på diagnosetidspunktet for stadium IV sygdom. 75 patienter havde symptomgivende metastaser på diagnosetidspunktet for cerebral metastasering. Der er signifikant forskel i overlevelse mellem patienter med symptomatiske vs asymptomatiske cerebrale metastaser: Median OS 5,0 måneder vs median OS ikke nået. Blandt patienter med asymptomatiske cerebrale metastaser fik alle systemisk behandling (overvejende checkpointhæmmer behandling). Blandt patienter med symptomgivende metastaser fik 43% ingen systemisk behandling. For disse patienter var median overlevelsen 2,9 måneder. Supplerende data fra 2015 vil blive præsenteret på mødet.

*Konklusion*

Hovedparten af patienter med cerebralt metastaserende melanom har symptomgivende metastaser på diagnosetidspunktet. Patienter med symptomgivende metastaser har en væsentlig ringere overlevelse end patienter med asymptomatiske metastaser.

**Clinical epidemiology + Database research****Abstract title****#129 Recurrence in Danish stage I lung cancer patients, assessing the follow-up program. Are we failing to identify patients with cerebral recurrence?****Presenting author**

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**Authors**

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**Abstract**

There is a paucity of evidence regarding the optimal follow-up (FU) regimen. Consequently, FU is organized differently across countries. The Danish FU regimen has relatively short FU intervals with a computed tomography (CT) scan every three months in the early phase (first two years), then every six months in the late phase of FU (3rd,-5th year). Characterizing recurrences missed by the FU program in terms of site, tumor histology, department and phase of FU, could improve the FU program.

*Design*

Retrospective population-based case-control study.

*Results*

We included 233 curatively treated stage clinical I lung cancer patients taking part in the FU program who had a recurrence. The majority of recurrences (n=197, 84%) were identified through the FU program (FU group). Among the 16% (n=36) diagnosed with recurrence outside the FU program (symptomatic group), 53% had recurrence involving the central nervous system as compared 3% in the FU group. The unadjusted odds ratio (OR) for having an isolated brain recurrence (IBR) in the symptomatic group was 52.3 (95%CI: 15.1 – 181.4) as compared to the FU group. The OR for having a symptomatic recurrence in the early phase of FU was 2.5 (95%CI: 0.7 – 8.7) compared to the late phase.

*Conclusions*

The FU program did not identify the majority of patients with IBR. Including cerebral imaging in the FU program may result in an earlier detection of brain metastases prior to the development of symptoms.

**Clinical epidemiology + Database research****Abstract title****#130 Localization of loco-regional recurrences after neoadjuvant treatment for locally advanced and inflammatory breast cancer****Presenting author**

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**Abstract***Introduction*

With advances in diagnostics, surgery, medical oncology and radiation therapy, loco-regional recurrence (LRR) of early breast cancer in Denmark is historically low with a 5 year risk of 1.6% for local and 0.8% for regional recurrence (DBCG-IMN study). However, much higher LRR rates have been reported for locally advanced breast cancer (LABC) and inflammatory breast cancer (IBC). For early breast cancer, ESTRO consensus guidelines for target volume delineation have been published. The purpose of this study is to determine whether these guidelines are appropriate for use in LABC and IBC.

*Materials and methods*

The study will describe detailed localization of primary LRR as well as LRR occurring after the diagnosis of distant metastases in a cohort of 186 patients consecutively treated for LABC and IBC at a single institution over a ten year period. All patients have received neoadjuvant taxane-containing chemotherapy as well as HER-2 targeted and hormone therapy where appropriate. Localization of LRR will be determined from patient records, including clinical photography, imaging studies and radiation therapy treatment plans. The results will be reported in accordance with the ESTRO consensus guidelines.

*Results*

The study is in progress. Results are pending and will be provided at the conference.

**Clinical epidemiology + Database research****Abstract title****#131 Nationwide implementation of robotic minimally invasive surgery for endometrial cancer increases survival and reduces complications****Presenting author**

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**Authors**

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**Abstract***Introduction*

Laparoscopic Minimally Invasive Surgery (LMIS) in endometrial cancer does not compromise survival and reduces postoperative complications compared to Total Abdominal Hysterectomy (TAH). However, LMIS of complicated surgical procedures is challenging. Implementation of Robotic Minimally Invasive Surgery (RMIS) may facilitate a transition from open to minimally invasive surgery thereby affecting the risk of severe complications and survival positively.

*Method*

Nationwide prospective data on women with early stage endometrial cancer who received surgery January 2005-June 2015 in Denmark were retrieved from the Danish Gynecological Cancer Database and linked with national registers. RMIS was gradually implemented. The individual woman was allocated to group 1 if operated before and to group 2 if operated after RMIS implementation in her county. Adjusted multiple regressions and multivariate Cox-regressions were used to compare severe complications and 5-year survival in group 1 versus group 2 and between surgical modalities in group 2.

*Results*

A total of 5,654 women were included. In multivariate analyses, being operated in Group 1 was associated with increased mortality (HR, 1.22; 95%CI 1.05-1.41) and increased risk of severe complications (OR, 1.38; 95%CI 1.10-1.73) compared with group 2. In group 2, TAH was associated with increased mortality (HR, 1.66; 95%CI 1.29-2.15) and increased complications (OR, 2.89; 95%CI 2.00-4.20) compared with RMIS. Restricted and adjusted analyses revealed increased survival following RMIS among women with high-risk disease (HR, 1.76; 95%CI 1.12 to 2.77).

*Conclusion*

The nationwide centralization and implementation of robotic surgical availability enabled a paradigm shift towards minimally invasive surgery that translated into increased survival and reduced risk of severe complications. A randomized trial is warranted to confirm the potential superiority of robotic minimally invasive surgery.

**Clinical epidemiology + Database research****Abstract title****#132 Use of vitamin K antagonists and prostate cancer risk: A nationwide, nested case-control study****Presenting author**

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**Abstract***Introduction*

Use of warfarin and other vitamin K antagonists (VKAs) has been suggested to reduce the risk of prostate cancer. As identification of cancer preventive effects of VKAs would have implications for the development of drugs to treat or prevent prostate cancer, we conducted a nationwide, nested case-control study on the association between VKA use and prostate cancer risk.

*Materials & Methods*

Using the Danish Cancer Registry, we identified all men aged 40–85 years with incident, histologically verified prostate cancer during 2005–2015. Population controls were age-matched 1:10 to cases using risk-set sampling. We estimated odds ratios (ORs) for prostate cancer associated with VKA use by conditional logistic regression, with three or more years of VKA use as our a priori main exposure. We adjusted for age and calendar time (by design), comorbid conditions (diabetes, chronic obstructive pulmonary disease, ischemic heart disease, congestive heart failure, and conditions that might contraindicate VKA use), use of drugs with suggested preventive effects against prostate cancer, and highest achieved education.

*Results*

We included 38 832 prostate cancer cases with a median age of 69 years. Among cases, 1089 (2.8%) had used VKAs for three or more years compared to 10 803 (2.8%) controls yielding a crude OR of 1.01 (95% CI, 0.95–1.08). Multivariable adjustment for covariates had limited influence on the association (OR, 1.03; 95% CI, 0.97–1.10). We observed no dose-response pattern (e.g. 5-10 years of VKA use: OR, 1.06 95% CI, 0.97–1.16).

*Conclusions*

We found no evidence of a reduced risk of prostate cancer associated with VKA use. Several anti-neoplastic mechanisms have been proposed for VKAs in relation to prostate cancer development, however, in view of our findings, it is questionable whether these translate to the clinical setting.

**Clinical epidemiology + Database research****Abstract title****#133 The Danish Gynaecological Cancer Database (DGCD) nursing monitoring the national quality of pre- and postoperative care****Presenting author**

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**Abstract***Introduction*

Access to valid data is essential to improve the post-operative outcome of gynaecological cancer surgery, and to ensure that complications or a poor general condition does not delay subsequent radio-chemotherapy and recovery for the individual patient. On this background, the Danish Gynecological Cancer Database (DGCD) established a nursing database in 2011 called DGCD Nursing. The aim of DGCD Nursing is to monitor the quality of pre- and post-operative care, and to generate data for research.

*Material and methods*

Real time data are entered by clinical nurses at all the national cancer centres in accordance with the data protection legislation. To ensure optimal evidence based care, national clinical guidelines are available online and the implementation and local adjustments of these are facilitated by local DGCD Nursing representatives.

*Results*

During 2011 – 2017, a number of 5726 patients were registered in DGCD Nursing; 5570 with a final diagnosis (156 missing). As the inclusion criteria have been gradually extended, the number of patients with a final diagnosis is increasing, up till now with national coverage of average 94%. At the moment DGCD Nursing holds a total of 436 variables that monitor central pre- and post-operative care elements such as mobilisation, nutritional status, pain score, vital functions, and psychosocial support.

*Conclusion*

At national level, DGCD offers a comprehensive overview of the total patient pathway within gynecological cancer surgery. In addition DGCD Nursing has added to the quality and implementation of evidence based pre- and post-operative care and supported formation of professional networks. With continued validation of data, DGCD Nursing constitutes a sound and unique basis for research within the field of pre- and post-operative cancer care.

**Clinical epidemiology + Database research****Abstract title****#134 Awareness and surveillance reduces head and neck radiotherapy treatment length****Presenting author**

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**Abstract***Purpose*

Treatment course length is of essential importance in radiotherapy of head and neck cancer patients. National guidelines prescribe a maximum course length of 41 days for moderate accelerated treatments, and 48 days for non-accelerated treatments. The purpose of this study is to measure the time from the first to last fraction in a cohort of head and neck cancer patients treated 2003-2017, and to evaluate the effect of increased awareness of the importance of treatment course length.

*Methods*

The study included 2,011 head and neck cancer patients treated between 2003-2017 to 66-68 Gy in 33-34 fractions and never re-irradiated. From 2011 the department scheduled QA and service on treatment machines outside clinical hours to reduce non-treatment days. In February 2016, a systematic weekly review of the planned treatment course was introduced, where total radiation treatment course length and schedule was checked. Patients with scheduled treatment violations are conferred with the oncologist and the treatment plan is rescheduled.

*Results*

The mean length of accelerated treatment courses was reduced from 40.9 days in 2007 to 38.3 days in 2017. For non-accelerated courses, the mean was reduced from 50.3 days in 2007 to 45.9 days in 2017, making the treatment approximately 2 Gy more effective due to the reduced repopulation of the tumour. Rescheduled QA and service reduced the fraction of treatment course time violations according to guidelines to less than 20% for accelerated treatments and to less than 40% for the non-accelerated treatments after 2011. The systematic review of treatment schedule reduced the fractions of treatment course time violations to 4% for accelerated treatments, and to 13% for the non-accelerated treatments. The surveillance alternates between two radiation therapists and takes 5-15 minutes per week.

*Conclusion*

Awareness and continual review of treatment schedules of head and neck cancer patients reduced the treatment course duration.



