DANSKE KRÆFTFORSKNINGSDAGE

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POSTER BOOK

Danish Comprehensive Cancer Center

ANSKE MULTIDISCIPLINÆRE CANCER GRUPPER DMCG.dk

INDHOLDSFORTEGNELSEN

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DAHANCA 27 - Transoral Laserassisteret Mikrokirurgi (TLM) ved T1aN0M0 glottiscancer.

Lyhne NM[1,3], Hald K[2], Kjærgaard T[3], Godballe C[4], Tvedskov J[5], Ulhøj B[6], Overgaard J[1], på vegne af DAHANCA

Afdl for Eksperimentel Klinisk Onkologi, Aarhus University Hospital[1] , Øre-, næse-, halskirurgisk afdeling Aalborg[2], Århus[3], Odense[4], Rigshospitalet[5]. Patologisk[6] afdeling, Århus.

Baggrund

T1a glottiscancer er en rygeinduceret kræftform lokaliseret på det ene stemmebånd uden indvækst i andre strukturer.

I Danmark behandles T1a stemmebåndskræft med strålebehandling (RT). Prognosen er god.

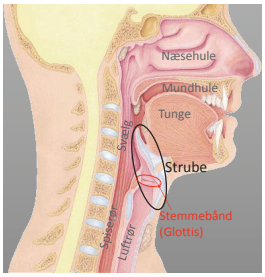
Nye kirurgiske teknikker med anvendelse af laser giver mulighed for skånsom kirurgisk fjernelse af T1a stemmebåndskræft.

Det er uvist om primær transoral laserassisteret mikrokirurgisk resektion (TLM) og primær accelereret RT er ligeværdige behandlinger af T1a stemmebåndskræft, når effekten måles på larynxbevaret (strubebevaret) overlevelse.

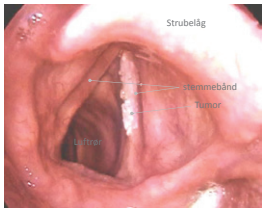
Det er også uafklaret om sygdomskontrol efter primærbehandlingen, stemmekvaliteten efter behandling, og behandlingsomkostningerne er ens ved TLM og RT.

Patienter, der primært behandles med RT, har forudgående fået foretaget et diagnostisk kirurgisk indgreb. Ved primær behandling med TLM er det muligt at foretage diagnostik og behandling i samme procedure, og patienten undgår de efterfølgende 5,5 ugers RT-behandling.

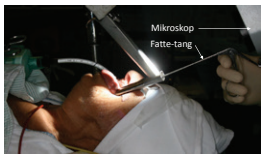
Hos patienter, der primært er behandlet med RT, er det som regel nødvendigt at foretage laryngectomi (strubefjernelse) ved recidiv. Patienter, der primært behandles kirurgisk, kan modtage RT ved recidiv og dermed bevare den naturlig stemmefunktion og luftvej.



Anatomisk illustration af struben, som adskiller svælget fra luftrøret. Stemmebåndene (glottis) er placeret midt i struben (Larynx). Stemmen genereres af stemmebåndene. Såvel sygdom på stemmebåndene som behandlingen heraf vil påvirke stemmen og medførende hæshed af forskellig grad og varighed.



Indblik med mikroskop i struben. Man kigger ind i struben oppe fra svælget, gennem stemmebåndene og ned i luftrøret. Der ses en T1a stemmebåndskræft lokaliseret fortil på højre stemmebånd. Kræften kan opereres med TLM eller behandles med RT.



Ved trans oral laserassisteret mikrokirurgi (TLM) foretaget i struben opereres patienten gennem et rør, der er ført gennem munden og ned i struben. Der anvendes fattetang til at stabilisere tumoren. Der anvendes laser som kniv. Kirurgen anvender mikroskop under proceduren.

Formål

At undersøge, om primær transoral laserassisteret mikrokirurgisk resektion, med mulighed for sekundær strålebehandling ved recidiv, er non-inferior i behandlingen af T1a stemmebåndskræft i forhold til primær behandling med accelereret strålebehandling.

Perspektivering

Studiet giver basis for at vurdere, om TLM skal indføres som behandlingstilbud i Danmark til patienter med T1a stemmebåndskræft.

Det er muligt, at primær behandling med TLM kan reducere andelen af patienter med T1a stemmebåndskræft, der laryngectomeres på grund af sygdomsrecidiv.

Indførelse af TLM kan bidrage til at danske patienter med T1a stemmebåndskræft tilbydes den - for den enkelte patient - mest optimale behandling under hensyntagen til sygdomskontrol, stemmefunktion efter primærbehandlingen og strubebevarelse.

Foreløbige resultater

Studiet lukkede for inklusion 1/5-2016. Den endelige analyse foretages, når alle inkluderede patienter har 60 måneders follow up.

	RT	TLM
Antal inkluderede	550	94
Median FU¤ (mdr.)	59	36
Recidiv	33 (6%)	5 (5%)
Laryngectomi#	24 (4%)	1 (1%)
TLM recidivbehandling	0	3 (3%)
Strålebehandling	550 (100%)	5 (5%) *
Inkurabelt recidiv	14 (3%)	1 (1%)

¤ FU: Follow up. # Laryngectomi : Strubefjernelse som medfører totalt stemmetab og behov for trachealkanyle.
* Strålebehandling er primær behandling for RT gruppen og recidivbehandling for TLM gruppen.

Metode

Design: komparativt fase II studie. To tidsmæssigt forskudte behandlingsgrupper sammenlignes.

Inklusion: Danske voksne statsborgere diagnosticeret med T1aN0M0 glottisk planocellulært carcinom og behandlet med enten kurativt intenderet accelereret strålebehandling i perioden 1/1-2003 til 31/8-2012 (n=550) eller radikal transoral laserassisteret mikrokirurgi i perioden 1/9-2012 til 1/5-2016 (n=94).

Follow up og analyse: Alle inkluderede patienter følges 5 år eller til dødsdato. Herefter opgøres studiets resultat. Der er indlagt interim-analyser af hensyn til patientsikkerheden.

Endepunkter: Det primære endepunkt er 5-års strubebevaret overlevelse. Sekundære endepunkter inkluderer: primær sygdomskontrol, sygdomskontrol med recidivbehandling, overlevelse, sygdomsspecifik overlevelse, strålebehandlingsfri overlevelse og stemmefunktion.

Selektionsbias: Er en udfordring i tidsforskudte studier, men kan i dette studie belyses, da alle ikke inkluderede patienter er registrerede i DAHANCA-databasen.

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QoLATI studiet - DAHANCA 34 protokol:
Et nationalt randomiseret forsøg med robotoperation versus strålebehandling til patienter med tidlige stadier af mundsvælgkræft

Channir HI[1], Rubek N[1], von Buchwald C[1] , Friborg J[2], Andersen E[2], Kjærgaard T[3]
Eriksen Grau J[4], Godballe C[5], Johansen J[6], Rønn Hansen C (Fysiker, QA)[6]

[1]Øre-næse-halskirurgisk afd., Rigshospitalet
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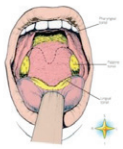
[5]Øre-næse-halskirurgisk afd., OUH
[6]Onkologisk afdeling, OUH

Introduktion:



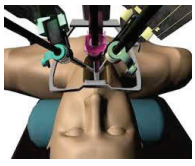
- Ca. 400 patienter diagnosticeres med mundsvælgkræft på årsbasis i DK
- Patienter med tidligt stadie mundsvælgkræft forårsaget af HPV er stigende i DK
- 5-årsoverlevelsen er >75%
- Standardbehandling er strålebehandling med eller uden kemoterapi. Behandlingen er ofte ledsaget af senfølger i form af mundtørhed og synkebesvær
- Transoral robotkirurgi (TORS) er ny robotassisteret behandling. Forhåbningen er at behandlingen er forbundet med færre senfølger sammenlignet med strålebehandling.

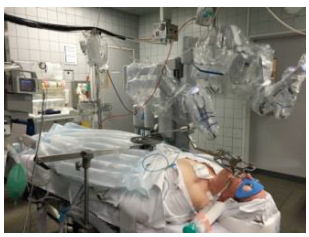
Hovedendepunkt:

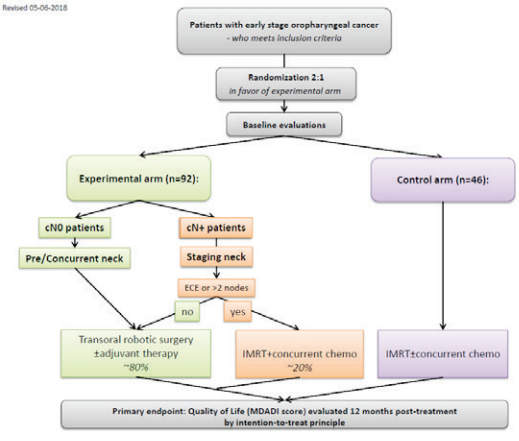
Patientrapporteret livskvalitet relateret til synkefunktion 12 måneder efter behandling

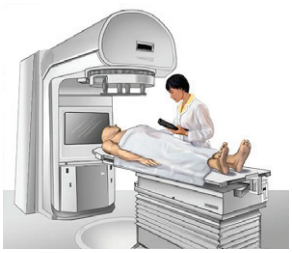
Metode:

- Inklusion af patienter med tidligt stadie mundsvælgkræft der findes operabel
- 3 centre: København (Rigshospitalet), Århus og Odense Universitetshospital
- 6 radioterapi centre: København (RH, Herlev), Århus, Odense, Aalborg og Næstved
- Randomisering imellem robotkirurgi og strålebehandling i forholdet 2:1
- Livskvalitetsmåling vha. patient-udfyldte skemaer (PROMs): MDADI, EORTC QLQ-H&N35, EORTC QLQ-C30
- Objektive synkefunktionsundersøgelser: barium kontrast og endoskopisk









The DBCG RT PBI trial: Accelerated partial breast irradiation for early stage breast cancer, early results from 882 patients enrolled in a clinically controlled randomized trial

Offersen BV[1, 2], Nielsen HM[2], Thomsen MS[2], Jacobsen EH[3], Berg M[3], Nielsen MH[4], Lorenzen E[4], Stenbygaard L[5], Jensen I[5], Petersen AN[6], Josipovic M[6], Jensen MB[7], Alsner J[1], Overgaard J[1]

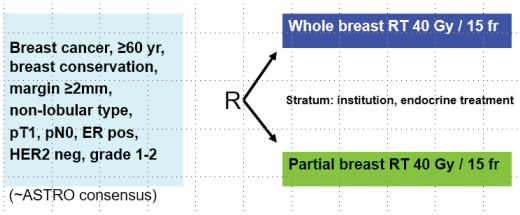
[1]Dept of Expt Clinical Oncology & [2]Dept of Oncology, AUH, [3]Dept of Oncology, Vejle, [4]Dept of Oncology, OUH, [5]Dept of Oncology, AAUH, [6]Dept of Oncology, RH, [7]DBCG RH

Purpose/objective

The risk of local recurrence is low in selected breast cancer patients, and most local recurrences appear in the index quadrant. Thus it may be acceptable to only irradiate the volume with the highest risk of recurrence, i.e. irradiate only part of the breast.
The aim of this randomized trial is to investigate differences in morbidity following whole breast and partial breast irradiation in patients operated with breast conservation for breast cancer with low risk of recurrence.
The hypothesis is that patients operated with breast conservation for breast cancer with low risk of recurrence can be treated with partial breast irradiation without experiencing more late radiation-induced morbidity compared with whole breast irradiation.

Materials and methods

Randomization



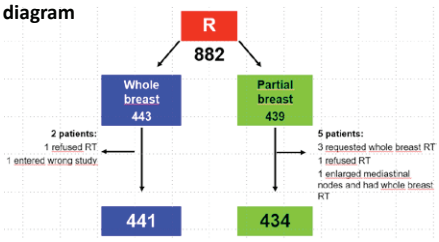
Endpoints

- Primary
  - grade ≥2 breast induration 3 years post RT
- Secondary
  - other RT-related morbidities
  - body image scale
  - patient satisfaction with therapy
  - pattern of recurrences
  - genetic risk profile for late RT-related morbidity

Baseline data, accrual 2009-2016

Center	Accrual
Aarhus	433
Vejle	161
Odense	116
Aalborg	91
RH Copenhagen	80
Dresden	1
Total	882

CONSORT diagram



Results

Patient and tumour characteristics

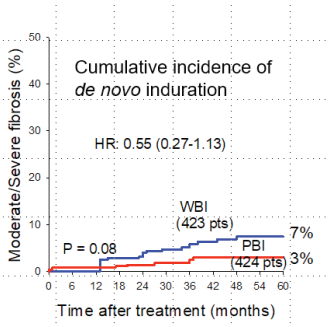
		Whole breast	Partial breast
Age	Median (years, range)	66 (60-86)	66 (60-83)
Tumour size	Median (mm, range)	10 (1-20)	10 (1-20)
Histology	Ductal Mucinous/Papillary/Tubular/other Lobular/DCIS	382 (87%) 52 (12%) 7	379 (87%) 52 (12%) 3
Grade	Ductal grade 1 Ductal grade 2	223 (58%) 155 (41%)	225 (59%) 150 (40%)
Breast size	Median cc (range)	664 (64-4257)	703 (72-2345)
Endocrine therapy	No Yes	190 (43%) 245 (56%)	186 (43%) 249 (57%)
Smoking	At baseline At 3 years	88 (20%) 46 (16%)	107 (25%) 54 (20%)
Charlson comorbidity	0 1, >1	72% 23%, 5%	80% 16%, 4%

Induration – Main analysis

3 years: whole breast 6%
partial breast 2%

4 years: whole breast 7%
partial breast 3%

Median follow up 3 years



There were significantly lower radiation doses to heart & lung using PBI, and no differences regarding dyspigmentation, telangiectasia, scar, edema, patient satisfaction and global cosmetic outcome.

Loco-regional and distant recurrences, other malignancy, death

	N	Whole breast	Partial breast
Local recurrence	6	2 LR# (1†)	4 LR€
Regional recurrence	2	0	2
Distant recurrence	4	1 (1†)	3 (3†)
Contralateral new primary	8	3	5
Other malignancy	34	14 (6†)	20 (5†)
Dead with no cancer	16	9	7

1 LR with syncronous regional rec and 1 LR with syncronous liver metastasis
€ 1 new primary cancer (different histology and another quadrant)
Total 5 of the 6 local recurrences were true local recurrences (same histology, located in the scar/area of the first cancer)

Conclusions

External beam forward planned IMRT partial breast irradiation based on 40 Gy / 15 is feasible
It causes lower radiation doses to heart and lung
There are few side effects at 3 years with no difference in breast induration, dyspigmentation, scar, edema, telangiectasia, global cosmetic ouitcome and patient satisfaction
There are few recurrences and not related to PBI
Since April 2016 it has been DBCG standard to selected patients

DBCG DANISH BREAST CANCER GROUP

The DBCG RT NATURAL trial: Accelerated partial breast irradiation versus no irradiation for early stage breast cancer, a clinically controlled randomized phase III trial

Offersen BV[1, 2], Al-Rawi S[3], Bechmann T[4], Kamby C[5], Matthiessen LW[6], Nielsen HM[2], Nielsen MH[7], Stenbygaard L[8], Jensen MB[9], Alsner J[1], Overgaard J[1]

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Purpose/objective

The risk of local recurrence is low in selected breast cancer patients, and most local recurrences appear in the index quadrant. Thus, external beam partial breast irradiation (PBI) 40 Gy/15 fr has been DBCG standard since April 2016 based on early results from the DBCG RT PBI trial and 5 year results from the UK IMPORT LOW trial. In these trials the local recurrence risk using PBI was <1% at 5 years, whilst the risk of contralateral new breast cancer was 2%.

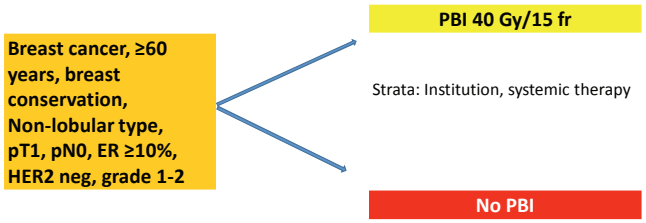
There are acute and late side effects from PBI, and it is important to balance the gains and risks from PBI.

The aim of this randomized trial is to investigate if omission of PBI in highly selected breast cancer patients is acceptable.

The hypothesis is that patients operated with breast conservation for breast cancer with low risk of recurrence can omit PBI without experiencing an unacceptable high risk of local recurrence at 5 years compared with patients treated with PBI.

Materials and methods

Randomization



Endpoints

Primary
Invasive local recurrence at 5 years

Secondary
Regional recurrence, Distant recurrence, Disease-free survival, Overall survival
Yearly morbidity scores:
Breast induration, Dyspigmentation, Scar, Telangiectasia, Global cosmetic score, Pain, Photographic evaluation of cosmesis, Patient satisfaction, Fear of recurrence

Participating centres

Denmark
Aalborg University Hospital, Aarhus University Hospital, Vejle Hospital, Odense University Hospital, Naestved Hospital, Herlev Hospital, Rigshospitalet
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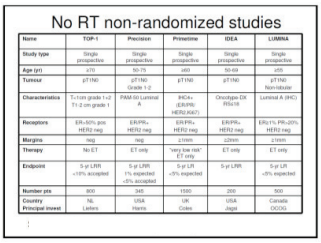
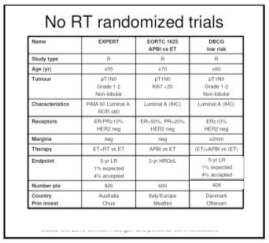
Studies on omission of radiation therapy





Studies on omission of adjuvant radiation therapy in selected patients.
The selection criteria in EXPERT trial and the DBCG RT Natural trial are similar, except in the DBCG RT Natural trial no PAM50 analysis is required, progesteron receptor not performed and systemic therapy follows DBCG guidelines, thus around 45% of the Danish patients will not have systemic therapy

Statistics

The statistics are based on early results from the DBCG RT PBI trial and 5 year results from the UK IMPORT LOW. In addition, the DBCG RT Natural trial is in harmony with the Australian EXPERT trial, and therefore the DBCG power calculation has also been influenced by that trial.
The 5 yr invasive local recurrence risk with PBI is expected 1%
The 5 yr contralateral new breast cancer risk is expected 2%
The 5 yr invasive local recurrence risk without PBI is accepted 4%
Based on 80% power, 2.5% one-sided sign level, 7% drop out, the number needed to include is calculated 926 patients, 463 patients in each arm.
The are 320 eligible patients in Denmark yearly.
An analysis of the local recurrence risk is planned when 200 patients have 2 yr follow up.

The trial stops accrual when 926 patients have been accrued. Based on results from the DBCG trial and other international trials, with results available at that time, the DBCG RT Committee will decide, whether omission of PBI is acceptable as DBCG standard in selected patients.

Current status

Ethical approval is pending. Danish departments start during the autumn 2018. A meeting is planned in Tromsø in November to initiate the trial in Norway

Conclusions

Since 2009 the DBCG RT Committee has actively improved the quality of adjuvant breast radiation therapy through several trials and studies.
The DBCG RT Natural trial is the next randomized trial to further individualize therapy. The trial is a natural extension of the findings in the DBCG RT PBI trial.
All Danish and several Norwegian deparments will participate
Results from this and other DBCG RT trials will help further optimize RT of early breast cancer

CIRRO

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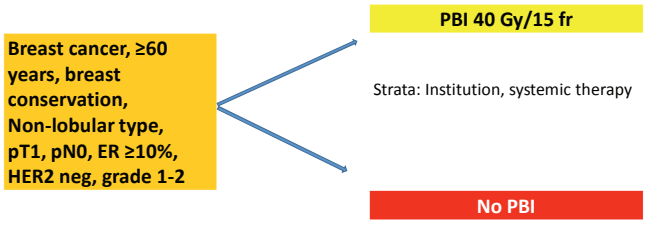

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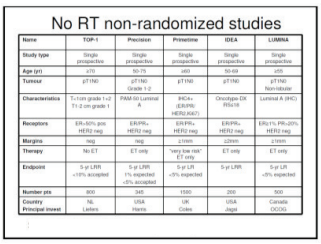

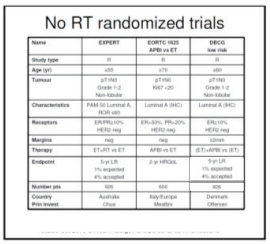

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Conclusions

Since 2009 the DBCG RT Committee has actively improved the quality of adjuvant breast radiation therapy through several trials and studies.
The DBCG RT Natural trial is the next randomized trial to further individualize therapy. The trial is a natural extension of the findings in the DBCG RT PBI trial.
All Danish and several Norwegian deparments will participate
Results from this and other DBCG RT trials will help further optimize RT of early breast cancer

Introducing Minimal Invasive Oesophagectomy in A Multi-disciplinary Tertiary Referral Centre

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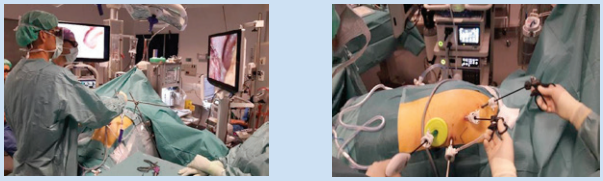
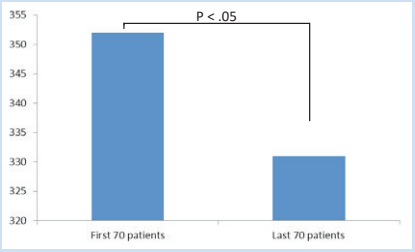
Introduction:
Minimal invasive oesophagectomy (MIO) in cancer patients has gained increasing popularity over the past 5 years because of reduced blood loss, lower total morbidity and respiratory complications, and a long term survival at least equivalent to the results after open resection.
This study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

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.

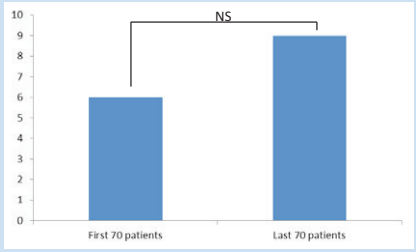


MIO (abdominal part: left, thoracic part: right)

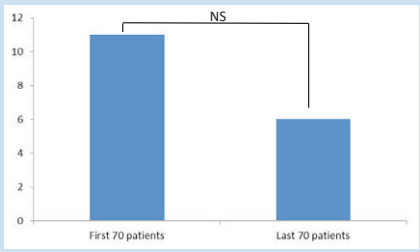
Results:
140 procedures were performed (23 November 2015 to 1 February 2018).
There were 19 women and 121 men. Median age was 67 years (range 16-83 years).



Mean procedure time (minutes)



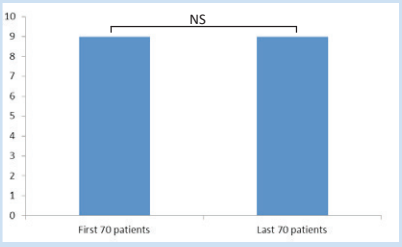
Risk of conversion to open procedure (%), abdominal part



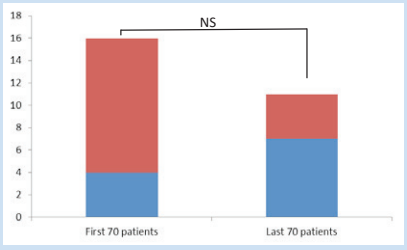
Risk of conversion to open procedure (%), thoracic part

T-stage	Number of patients	N-stage	Number of patients
T0	18	N0	78
T1	26	N1	32
T2	22	N2	19
T3/T4	73	N3	11

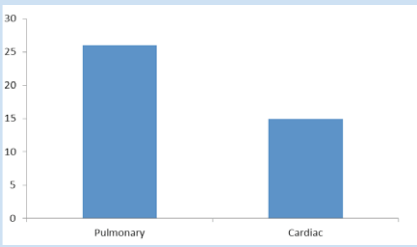
Pathologic T-and N-stage



Length of postoperative stay (days)



Risk of anastomotic leakage (%)
blue: patients with need for endoscopic/surgical treatment



Medical complications, all patients (N)

30 day mortality rate: 3% . 1 year survival rate : 83%.

Conclusion:
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.

Conflict of Interest:
None

Region of Southern Denmark
OUH Odense University Hospital

University of Southern Denmark

Beating cancer cachexia

A multimodal, cachexia-preventing intervention in patients with non-small cell lung cancer (LUCANU-2)

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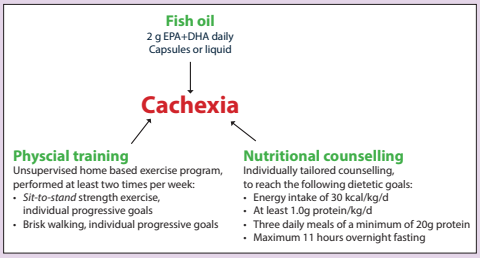
** Department of Oncology, Aalborg University Hospital

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

- Feasibility intervention study
- 70 patients with inoperable NSCLC
- Observational period from 1st to 4th cycle of systemic anti-neoplastic treatment (chemotherapy or immune-checkpoint inhibitor)
- Multimodal intervention with physical training, nutritional counselling and fish oil



Measurements

- Body weight, dietary intake and physical function 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, to assess feasibility of the study protocol: accrual rate, attrition rate and adherence to protocol.
- Secondary outcome; body weight changes, muscle mass and physical function. Secondary outcomes will be compared to a historical control 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.

AALBORG UNIVERSITY HOSPITAL
Denmark

Sikkerheds- og effektstudie af standard dosering af Carboplatin hver 3. uge plus daglig Navelbine® 20/30 mg (oral) i løbet af 4 cykler (12 uger) til behandling af fremskreden NSCLC; Et pilot studie

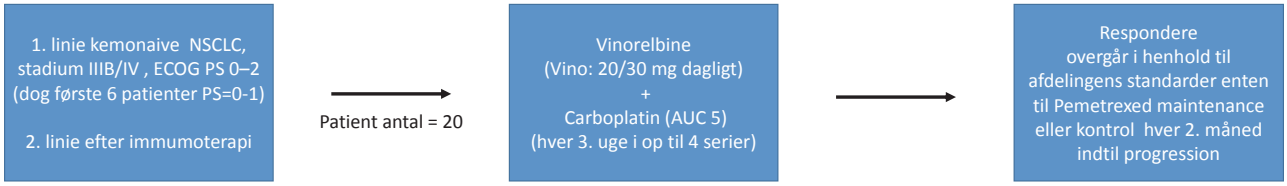
Maria Kandi[1)]; Peter Meldgaard[1)]
[1)]Kræftafdelingen, Aarhus Universitets Hospital, Danmark

Baggrund
Lungekræft er en af de mest hyppigste kræfttyper i Danmark. Incidensen for årene 2011-2015 er omkring 4596. Uhelbredelig lungekræft er en alvorlig sygdom med en middel overlevelsestid på mellem 10 og 14 måneder efter diagnosen stilles, trods behandling med kemoterapi. Målet for behandling af patienter med metastatisk ikke-små-celle lungekræft (NSCLC) er at lindre symptomerne, 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 for at opnå lavere behandlingsrelateret toksicitet samtidig med at opretholde eller endog forbedre effekten. Hypotesen er at de hyppige administrationer bl.a. medfører at tumorcellerne bliver eksponeret kontinuerligt for lægemidlet, og at deres evne til regenerering mellem kemoterapi-serierne hæmmes, medførende bedre tumor kontrol.

Primært mål
At undersøge Navelbines bivirkningsprofil og tolerabilitet (grad 2-5 CTC), når denne gives som lille daglig dosis (metronomisk) sammen med Carboplatin AUC 5 hver 3. uge.

Metode
Projektet vil inkludere 20 patienter med inkurabel lungekræft, som er kandidater til 1. linie standard kemoterapi (PDL-1 < 50 %). Inklusionen er påbegyndt d. 1. april 2018 på kræftafdelingen på AUH. Studiet er investigator initieret og designet som et ikke-randomiseret prospektivt studium med en arm. Patienterne bliver tilbudt standard kemoterapi i form af Carboplatin AUC 5 (iv. hver 3. uge) og metronomisk kemoterapi i form af kapsel Navelbine® i små doser (20/30 mg) dagligt i 12 uger, efterfulgt af en evaluering af behandlingen i henhold til afdelingens standarder. Der gives fire serier kemoterapi. Under 1. serie gives 20 mg Navelbine dagligt, hvis denne dosis tolereres uden grad 3-4 toksicitet, øges dosis i efterfølgende serier til 30 mg dagligt i resten af behandlings perioden. Patienterne registrer deres bivirkninger online via ambuflex® hver 3. uge i 12 uger. Der foretages interimanalyse efter 10 patienter.

Studie design



Konklusion
Studiet er et af de første studier, hvor der gives Carboplatin i standard regime sammen med Navelbine i metronomisk dosering dagligt uden pause i 12 uger hos patienter med NSCLC. Vi har indtil nu inkluderet 7 patienter. Den første patient har netop afsluttet fire behandlings serier (inkl. 20 mg Navelbine dagligt i 12 uger), med partiel respons og har valgt at overgå til kontrol med CT-scanninger hver 2. måned.

Vi håber at forsøgsresultaterne kan hjælpe os med, i nær fremtiden, at designe randomiserede studier med metronomisk behandling til lungekræft patienter, hvor vi nedbringer bivirkningerne af vores standard kemoterapi og måske endda øger behandlings effekten.

SENTIREC ENDO

Sentinel Node Mapping with Robotic Assisted Near Infra-red Fluorescent Imaging in Women with Endometrial Cancer

Sara Elisabeth Sponholtz[1,2], Ole Mogensen[1,3], Malene Grubbe Hildebrandt[2,4], Doris Schledermann[5], Thiusius Rajeeth Savarimuthu[6], Pernille Tine Jensen[1,2]

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[2] Institute of Clinical Research, University of Southern Denmark.
[3] Department of Obstetrics and Gynecology, Karolinska University Hospital, Sweden.
[4] Department of Nuclear Medicine, Odense University Hospital, Denmark.
[5] Department of Clinical Pathology, Odense University Hospital.
[6] The Maersk McKinney Moeller Institute, University of Southern Denmark.

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:

1. The effect of SN mapping on the incidence of lymphedema in women with early stage endometrial cancer.

2. 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

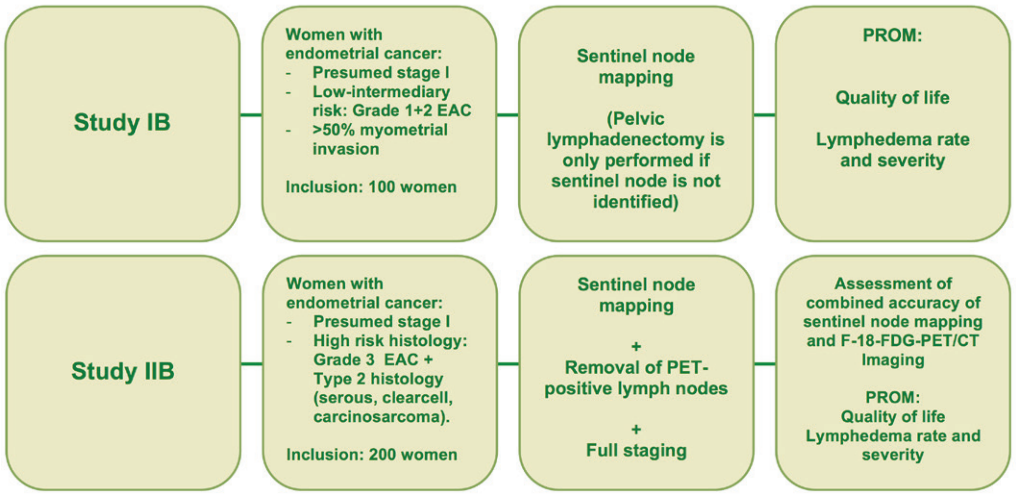


Figure 2: Overview of the two sub-studies in SENTIREC ENDO.

Results

- Four gynaecologic oncology centres in Denmark are participating in this project.
- Three centres have completed the pilot study where a total of 104 patients were included, showing an overall SN detection rate of 92.3%, hereof 71.2% bilaterally.
- In Study IB, 12 of 100 patients with FIGO IB endometrial cancer have been included (along with 84 patients with FIGO IA). In Study IIB, 34 of 200 patients with high-risk endometrial cancer have been included.

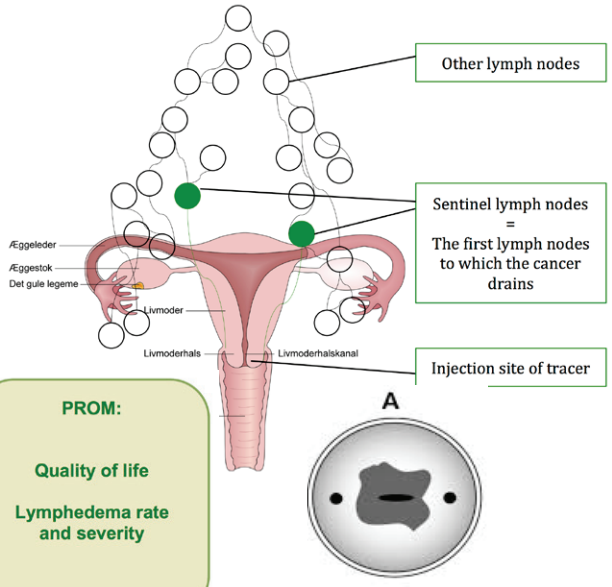
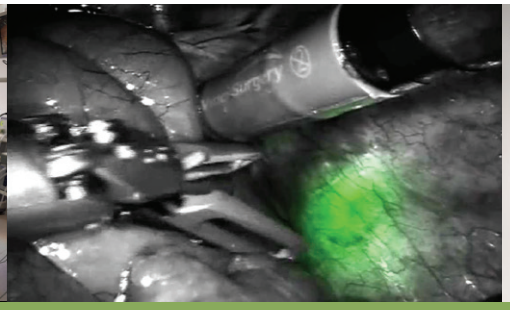


Figure 1: Sentinel node mapping and injection site of indocyanine green in the cervix.

Conclusion

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



OUH
Odense University Hospital
Svendborg Hospital

Maersk Mc-Kinney
Moeller Institute

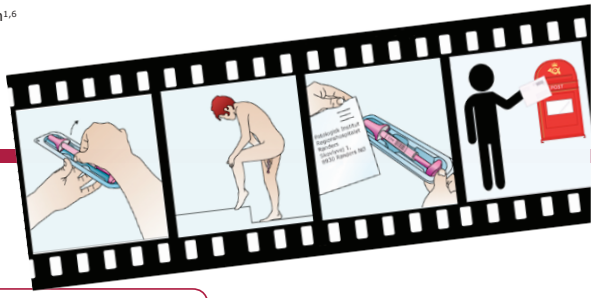
Kræftens Bekæmpelse

SDU

HPV self-sampling in cervical cancer screening

Mette Tranberg[1], Bodil Hammer Bech[2], Jan Blaakær[3], Hans Svanholm[4], Jørgen Skov Jensen[5], Berit Andersen[1,6]

1) Department of Public Health Programmes, Randers Regional Hospital, Denmark
2) Department of Public Health, Section for Epidemiology, Aarhus University, Denmark
3) Department of Obstetrics and Gynaecology, Odense University Hospital, Denmark
4) Department of Pathology, Randers Regional Hospital, Denmark
5) The State Serum Institute, Copenhagen, Denmark
6) Department of Clinical Medicine, Aarhus University, Denmark



Take home messages

- Compared with both the opt-in and control groups, sending HPV SS (self-sampling) kits directly to all non-participants was the most successfull strategy in terms of increasing screening participation and attracting unscreened women into screening
- Implementation of HPV SS could increase the overall screening participation among invited women aged 30-64 years by 2 to 5%, thereby improving cervical cancer prevention
- Cytology-triage by the general practitioner (GP) was suitable

Background

- In the Central Denmark Region, the overall screening participation is 68% among women aged 30-64 years; yet, 45% of all newly diagnosed cervical cancers are found among underscreened women
- Offering home-based HPV SS to non-participants may increase screening participation
- However, the offer of a HPV SS kit (opt-in) has been reported to be less effective than sending the kit directly to all women (directly mailed)

Aim

- To evaluate the effect on participation of direct mailing and timely opt-in approaches for offering HPV SS to non-participants compared with a standard second reminder for regular cytology screening
- To measure the compliance to cytology-triage among HPV positive self-samplers

Methods

- Randomized controlled effectiveness trial

Outcomes:

- Participation rate 180 days post intervention (reported as intention-to-treat)
- Compliance to cytology-triage by the GP within 90 days post test results

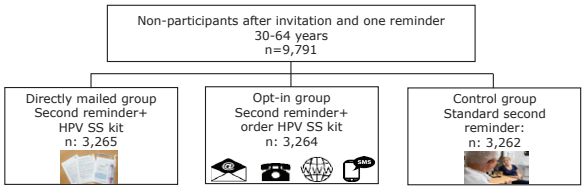


Fig. 1: RCT design overview. HPV SS kit: HPV self-sampling kit

Results

- The participation rate after the second reminder was significantly higher in the directly mailed group (38.0%) than in the opt-in group (30.9%) (participation difference (PD): 7.1%, 95% CI: 4.8-9.4%) and the control group (25.2%) (PD: 12.8% 95% CI: 10.6-15.0%)
- Compared with the control group; the directly mailed strategy made signficantly more unscreened women participate in screening (7.2% versus 19.9%, PD: 12.6%, 95% CI: 8.8-16.4%). The opt-in strategy had no significantly effect (8.7%, PD: 1.5%, 95% CI: -1.6-4.6%)
- Effect on the overall screening participation
  - Opt-in: from 69 to 71%
  - Direct mailing: from 69 to 74%
- The compliance to follow-up among self-samplers:
  - ≤ 90 days: 90.7%, 95% CI: 83.9-95.3%

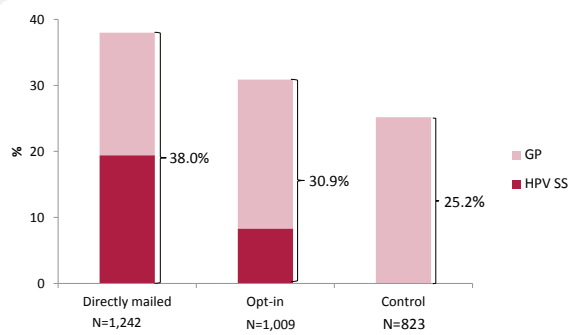


Fig. 2: Participation rate in each group after the second reminder

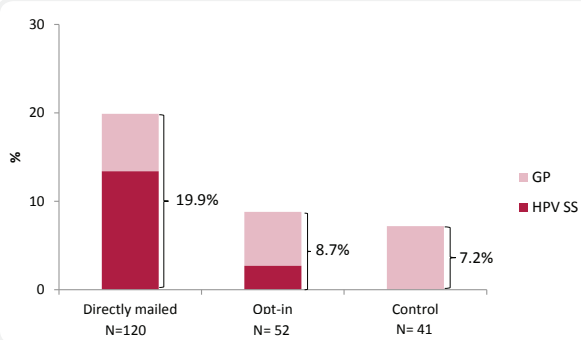


Fig. 3: Participation rate in each group after the second reminder among unscreened women*

*) No cervical cytology sample registered within the previous 7-15 years depending on the woman´s age

Funding: The Health Research Fund of Central Denmark Region; The Health Foundation; The LSB Foundation; The Family Nielsen´s Foundation; The Krista and Viggo Petersen´s Foundation; The Aragon Foundation
Competing interests: Axlab, the Danish manufacturer of Evalyn Brush; and Roche, the manufacturer of the Cobas® 4800 HPV DNA assay provided self-sampling devices and test kits for the study, respectively.

SIGNAL INTENSITY CHANGE ON T2WI AS DIAGNOSTIC MARKER FOR GLIOBLASTOMA

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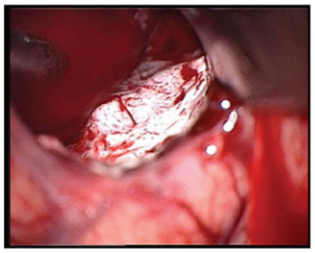
[1] Department of Neurosurgery, Odense University Hospital, University of Southern Denmark
[2] Faculty of Health Sciences, University of Southern Denmark

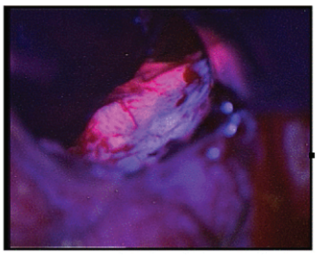
INTRODUCTION

Patients with glioblastoma (GBM) has a median survival of 12-15 months. Histopathology is essential for treatment. A non-invasive diagnostic method is therefore needed for patients unable to undergo surgery and, in the future, for research in to neoadjuvant chemotherapy.

5-aminolevulinic acid (5-ALA) is selectively taken up, synthesized and accumulates as PpIX in GBM cells. PpIX can be visualized during microscopical surgery as fluorescent red light.

Hypothesis: Uptake of 5-ALA in GBM cells can measured on T2 weighted MRI





GBM under white light and under BLU filter, emitting red light

METHODS

Descriptive study including patients undergoing surgery for recurrent GBM.
Patients underwent standard MRi on the day before and on the day of surgery. On the day of surgery 5-ALA was orally ingested three hours prior to the scan.
Surgeons graded fluorescence as strong, weak or none during surgery.

On every scan, regions of interest (ROIs) were identified and signal intensity (SI) was measured. As SI is variable and depended on MRI scanner etc. it is not quantifiable by itself. Therefore a ratio using the mean SI of contralateral "intact" white matter was used. The mean SI ratio of tumor tissue on T2 weighted imaging (T2WI) before and after ingestion of 5-ALA was compared. Ipsilateral oedematous tissue was used as a control.

RESULTS

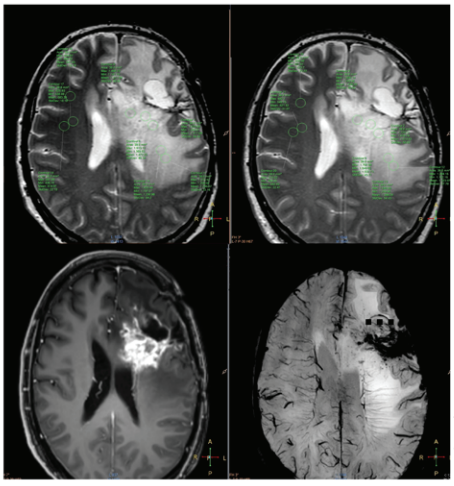
Three patients were included. Fluorescence was graded strong in all.
Signal intensity from pre- (1.95 +/- 0.06, 95% CI) and post-5-ALA ingestion (2.05 +/- 0.06) was significantly different, $p<0.001$. Oedematous tissue signal intensity pre- (2.02 +/- 0.06) and post (2.04 +/- 0.05) was not significantly different, $p=0.25$.

No significant difference in contralateral white matter was observed. No adverse effects were registered.

Patient			Observations	Signal intensity ratio +/- SE	CI*	P-value
Total	*5-ALA*	*Pre*	45	1.95 +/- 0.06	1.84 - 2.07	**< 0.001**
		Post	45	2.05 +/- 0.06	1.92 - 2.17	
	Oedema	*Pre*	30	2.02 +/- 0.06	1.90 - 2.13	**0.25**
		Post	30	2.04 +/- 0.05	1.94 - 2.14	

CONCLUSION

The preliminary studies show that 5-ALA can be visualized on T2WI in 5-ALA positive tumors. However, more patients are needed to increase statistical certainty.
Currently, inclusion of further patients is being arranged in collaboration with international partners.



Top: T2 before and after 5-ALA incl. ROIs
Bottom: T1 and SWI

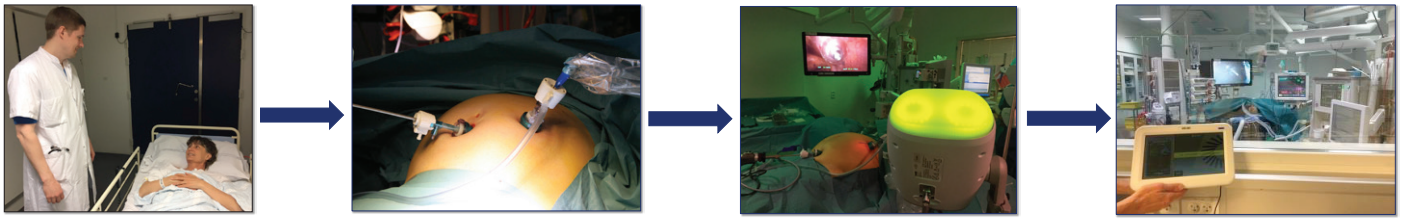
OUH Odense University Hospital

PIPAC (Pressurized IntraPeritoneal Aerosol Chemotherapy) in the prevention and treatment of peritoneal metastasis

Graversen M, Asmussen J, Detlefsen S, Fristrup C, Pfeiffer P, Ploug M, Mortensen MB

INTRODUCTION

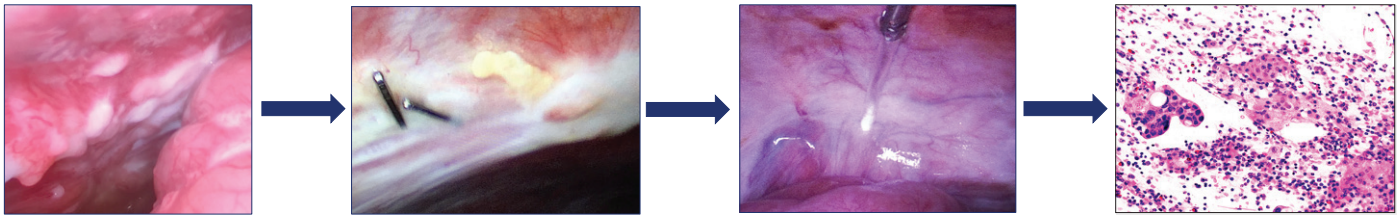
Peritoneal metastasis (PM) represents end stage disease in many types of cancer and systemic chemotherapy has limited effect on PM. Curative treatment of PM is only possible in a highly selected fraction of patients, and the majority of patients with PM will die within six months from diagnosis. Realizing 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.



METHOD

PIPAC is a new technique where aerosolized chemotherapy is emitted directly inside the abdominal cavity during laparoscopy[1]. 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[2].



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 adverse reactions were seen and the majority of patients were discharged within 24 hours[2,3]. 72% (50/69) of the patients had >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, and patients are referred from both abroad and other Danish regions.

[1]*Solass et al. Ann Surg Oncol 2014*
[2]*Graversen et al. Ther Adv Med Oncol 2018*
[3]*Graversen et al. Pleura & Peritoneum 2016*

OUH Odense University Hospital

Region of Southern Denmark

University of Southern Denmark

National status på implementering af MDT-konferencen - deltagernes perspektiv

For første gang foreligger en videnskabelig undersøgelse om danske MDT-konferencer

Introduktion

MDT-udvalget undersøger, under DMCG.dk's kommissorium for udvalget, status for implementering af MDT-konferencen og udvalgets retningslinje *Multidisciplinær kræftbehandling – en vejledning til MDT-konferencen* fra 2016. MDT-udvalget har valgt en videnskabeligt baseret tilgang fremfor en markedsorienteret. Evalueringen identificerer såvel vellykkede initiativer som udfordringer, samt udviklingsområder for MDT-konferencerne, ud fra individuelle oplevelser.
I undersøgelsen indgår MDT-deltagere indenfor de fire kræftsygdomme med størst patientvolumen:
Lungecancer, prostatacancer, mammacancer og kolorektalcancer.

Konklusion

MDT-konferencen er mange steder veletableret og velfungerende. De mange eksempler på patientforløb, der kvalificeres ved konferencen, grundfæster vigtigheden af det tværfaglige samarbejde og illustrerer, hvor der stadig er plads til forbedring.
Data giver anledning til
- **mange diskussioner, og**
- **dokumenterer hvordan konferencerne har afledte effekter i form af bl.a. tættere samarbejdsrelationer.**

Den kvalitative metode har resulteret i
- **Ord og eksempler på både det helt unikke og positive ved konferencerne**
- **Ord på udfordringer, samt**
- **Identificeret et reelt udviklingspotentiale.**

Afvikling af konferencen

"God forberedelse vil give en bedre besvarelse og hurtigere afvikling af konferencen. I nogle tilfælde når billederne ikke frem i tide og konferencebeslutningen må flyttes til næste konference – i sådanne tilfælde vil en optimal billedoverførsel betyde, at behandlingsbeslutninger ikke forsinkes med flere dage."

"Hvis teknikken virker, vil det betyde hurtigere afvikling af MDT og ikke mindst større tilfredshed hos alle. Det er meget frustrerende at skulle bruge tid på noget, der ikke fungerer, og det er utilfredsstillende for de regionale afdelinger, der er med på videokonference, at de ikke kan se billeder."

"Det har stor betydning for såvel afviklingen, som kvaliteten af behandlingsbeslutningen, hvor godt oplægget er. Nogle afdelinger formår at skrive meget struktureret og medtage væsentlige kliniske oplysninger, andre er mere i prosaform/snakkende og man skal tygge sig igennem oplægget for at uddrage det væsentlige – hvis det er der."

Fremtidsperspektiver for MDT-konferencerne

Nationale audits på konferencebeslutninger

Koordinering af patientforløb for patienter med konkurrerende cancerdiagnoser

Uddannelsespotentiale

"Det er betydningsfuldt for de uddannelsessøgende, fordi diskussionerne ved MDT-konferencen kan give et godt indblik i, hvor kompleks brystkræftbehandling i virkeligheden er."

"Jeg synes uddannelsesmulighederne forsømmes groft – konferencen falder sammen med ambulante patienter og dermed ofte umuligt at deltage for H-læger."

"Vi har desværre ingen uddannelsespladser for brystkirurgi på vores matrikel, og de plastikkirurgiske uddannelseslæger har desværre ikke det privilegium at følges med brystkirurgerne."

Afledte effekter af konferencen

"Man kender hinanden på tværs af specialer, det betyder at det er betydelig lettere at tage telefonen og få afklaret patientrelaterede ting ved behov. Vi underviser vores yngre kolleger på tværs af specialer, har kendskab og interesse for fælles patienter."

"Fik snakket med en af mine samarbejdskollegaer fra MDT-konferencen. Vigtigt, fordi jeg fik primet min kollega til jeg vil kontakte ham og hvorfor og fik en meget positiv reaktion☺ Nu vil jeg planlægge, hvilke punkter vil kan diskutere, når vi mødes."

Beslutningens kvalitet

"Vi har fået en meget større grad af ensartethed i behandlingen af vores patienter, samtidig med at der er åbnet op for diskussion af tvivl og vanskelig beslutningstagen uden at nogen bliver hængt ud eller latterliggjort."

"Ledelsen virker ikke til at have forståelse for, hvilken betydning MDT-samarbejdet har for behandling/diagnostik af patienten, og kan ikke sætte sig ind i, hvorledes mine kollegaer på patologiafdelingen og jeg opfatter det, som en stor og vigtig del af vores arbejde, som i høj grad også er med til at effektivisere det daglige arbejde. MDT konferencerne øger til stadighed vores viden og forståelse af kollegaers arbejde, behandlingsmuligheder for patienten og skærper dermed vores svarafgivelser til gavn for patienten og kollegaer."

"Hvis vi har ordentlig planlægning og synlighed omkring opgaven, vil grundlaget for MDT-beslutningerne blive bedre til gavn for både patienten og sundhedsvæsnet. Kirurger, der kaldes på operationsgangen midt i det hele, bliver ringet op og render frem og tilbage, fordi de skal være flere steder på een gang, bidrager ikke med kontinuitet og koncentration - forståeligt nok i øvrigt. Dårlige/ingen oplæg betyder, at vi er meget længe om at danne os overblik over patientens samlede situation og behov - det tager tid fra konferencen til ordentlige diskussioner og øger risikoen for fejl, fordi vigtige detaljer måske overses. Samtidig med er det tidskrævende uden at bidrage med proportional kvalitet."

"Jeg deltager via telefon og det er meget forstyrrende, at der er så meget larm i baggrunden, og man går glip af noget af kommunikationen ved ikke at se de andre."

Oversigt respondenter	
Lungecancer	
Potentielle resp.	112
svarprocent	42,86
Kolorektal cancer	
Potentielle resp.	283
svarprocent	24,73
Mammacancer	
Potentielle resp.	144
svarprocent	37,9
Prostata cancer	
Potentielle resp.	79
svarprocent	19,28
Total på de fire sygdomsgrupper	
Potentielle resp.	618
Antal besvarelser	189
Total svarprocent	30,6

Materiale og metode

Undersøgelsens metode baserer sig på en tilgang, der inddrager såvel kvantitative som kvalitative spørgeskemadata. Den konkrete teknik hedder Most Significant Change-metoden (MSC). Data analyseres med softwaren NVivo.
- **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 *Multidisciplinær kræftbehandling – en vejledning til MDT-konferencen*.**
- **Validitet er sikret via**
  - **pilottestning i udvalgets egne MDT-konferencer samt**
  - **ved forskertriangulering, idet kodning foretages induktivt af tre medlemmer af udvalget og valideres af udvalget.**

Målgruppe:
- **MDT-deltagere indenfor lunge-, prostata-, mamma- og kolorektalcancer er inkluderet og har modtaget spørgeskema pr. mail gennem egen MDT-leder.**
- **Strategi**
  - **Spørgeskemaer er udsendt til MDT-ledere og kontaktpersoner 24. april 2018, og af disse sendt videre til deres respektive MDT-konferencemedlemmer.**
  - **Efterfølgende er der rykket fire gange, senest medio juni med svarfrist 28. juni. Svarprocenten på knap 31 % betyder, at der ikke kan generaliseres; data tillader derimod analytiske konklusioner hvad angår MDT-deltagernes erfaringer og tanker om MDT-konferencen.**

Resultater

Kodning og analyse pågår aktuelt og forventes afsluttet senere i år.

Overordnet viser de præliminære resultater, at
- **MDT-konferencen er en veletableret del af den kliniske hverdag.**
- **Konferencerne kvalificerer behandlingsforløbene væsentligt.**
- **Konferencerne er mange steder udfordret af mangelfuld koordination og afvikling af konferencen, ligesom tid til forberedelse, deltagelse og opfølgning ikke opleves tilstrækkelig.**
- **Uddannelseslæger deltager i begrænset omfang og i nogle tilfælde alene, hvilket betyder på den ene side at uddannelsespotentialet er dårligt udnyttet, på den anden side at afgørende beslutninger træffes uden den nødvendige ekspertise.**

Forfattere: Dehn P, Hillingsø J, Hagemann-Madsen RH, Asmussen JT, Petersen LN, Lajer H, Rasmussen T, Borre M, Boolsen MW, Lundvall L

#47

Costs and consequences of introducing robotic surgery for women with gynecological cancer

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Purpose

To evaluate the costs and consequences of Robotic Surgery compared to open access and conventional laparoscopy in women with endometrial cancer

Background

- The demand for more advanced medical technologies is growing.
- Robotic surgery is the latest technology and assumed to be more expensive in the short-run compared to laparoscopy and open hysterectomy.
- This study will include all work- and health related costs and consequences associated with different surgical procedures in women with early-stage endometrial cancer (FIGO stage I-II).

Methods

The study consists of 3 parts:

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

Part 2: Evaluation of endpoints between the control and intervention group

- Length of stay
- No. of re-operations
- Returning to labor market
- Visits at General Practitioner and Doctor at emergency
- Total costs from hospitalizations, secondary healthcare- and all medicine used one year before and after surgery

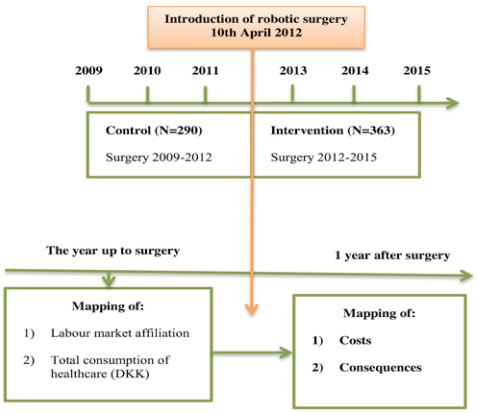
Figure 2: Length of stay

Length of stay, day	Mean
Control	2.7
Intervention	1.7

Figure 3: No. of reoperations 1 year after surgery

No. of re-operations	Control (n=290)	Intervention (n=363)
1	8 (2.8%)	9 (2.5%)
2	4 (1.4%)	-
3	-	6 (1.7%)
Total	12 (4.2%)	15 (4.2%)

Figure 1: Method of part 2



Tables of the status 1 year before and after the surgery

Figure 4: Working status

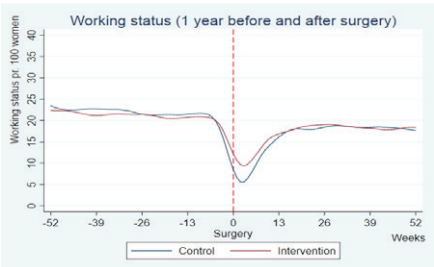


Figure 5: Sickness benefit

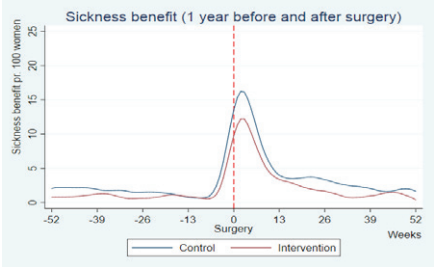
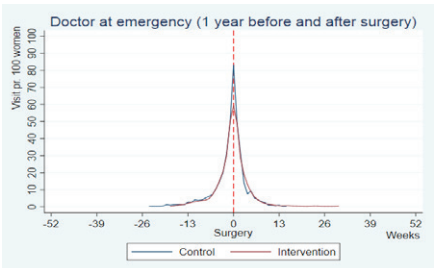


Figure 6: Visit at General Practitioner

Figure 7: Visit at Doctor at emergency



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UNIVERSITY OF SOUTHERN DENMARK

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

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Conclusion

OPAC is the first officially supported multi-disciplinary Danish research center focusing on PC. It seems possible to initiate and sustain a broad multi-disciplinary environment that can explore new translational research pathways. 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

Introduction

Pancreatic cancer (PC) patients have an extremely poor prognosis, and the median overall survival for Danish PC patients is 6 months (*Fig. 1*). 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 true 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.

Process

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 overall goal of OPAC activities is *Personalized Medicine* in PC patients, and the first **OPAC** results[(1-5)] demonstrate the advantages of our multidisciplinary approach, providing mutual inspiration, support and collaboration.

Outcomes

Examples of ongoing **OPAC** directed PC studies are provided below:

1. Genetic markers predictive of Familial Pancreatic Cancer and Hereditary Pancreatitis (PhD study)

2. Treatment of locally advanced and metastatic pancreatic cancer (PhD study)

3. Subtyping of pancreatic cancer-associated fibroblasts (PANCAF): Analysis of their value as prognostic markers and as targets for the development of stroma-modulating therapeutic strategies (PhD study)(*Fig.2*)

4. Large scale genomic analysis of circulating tumor DNA for non-invasive detection of early-stage pancreatic cancer, residual disease and recurrence (PhD study)*(Fig.2)*

5. Pancreatic core-needle biopsies obtained by endoscopic ultrasound (EUS): Role for the precise pre-therapeutic diagnosis of pancreatic cancer, and as tool to obtain tissue specimens for research

Fig. 1
Kaplan-Meier survival curve for Danish PC patients (DPCD Annual Report 2017)

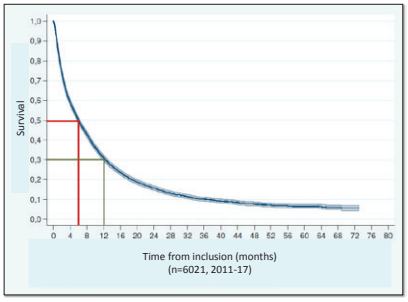
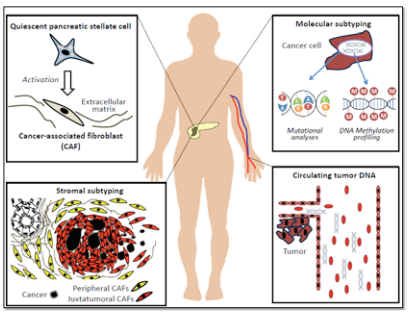


Fig. 2
Examples of ongoing OPAC directed research in PC patients



OPAC references

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2) Graversen M, Detlefsen S, Bjerregaard JK, Fristrup CW, Pfeiffer P, Mortensen MB. Prospective single-center implementation and response evaluation of pressurized intraperitoneal aerosol chemotherapy (PIPAC) for peritoneal metastases. Ther Adv Med Oncol. 2018 Jun 1;10:1758835918777036
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Karina Olling[1], Troels Bechmann[2,3], Poul Henning Madsen[3], Erik Hugger Jakobsen[2], Dorte Beth Toftdahl[2], Ole Hilberg[3,5], Angela Coulter[1,4,5], Karina Dahl Steffensen[1,2,3]
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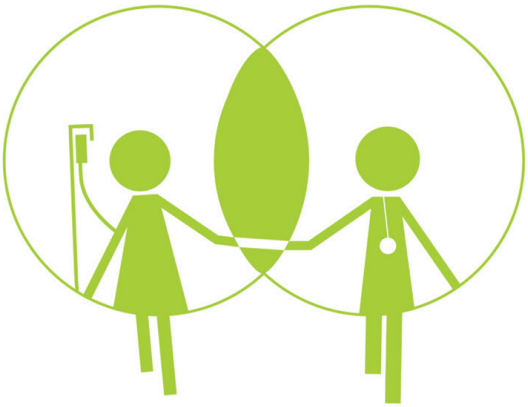
Danish Cancer Research Days
Aug. 30.-31., 2018

DEVELOPMENT OF A PATIENT DECISION AID TEMPLATE FOR USE IN DIFFERENT CLINICAL SETTINGS

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 to SDM such as lack of skills and lack of decision support. Patient decision aids (PtDAs) have been shown to be an effective and reliable support in the dialogue between patient and health care professional.



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.
Field testing of these prototypes with larger groups of patients and professionals is are currently being performed, and test of additional prototypes based on the PtDA template in different clinical settings is already going on.

AIM

The aim of this study was to develop and test a patient decision aid template and test two different prototypes designed to support SDM in adjuvant therapy for breast cancer and diagnostic work-up for suspicion of lung cancer.

The two decision topics were chosen to provide the best possible test and validation of the standard PtDA template, to ensure that the prototype 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.

Qualitative statements

"It requires an innovative thinking and courage of the physician to change work practice". - Physician

"The question is; How does the physician endure and accept the choice of the patient?" - Nurse

"It structures and models the consultation in a way that gives the best condition for actual influence on the treatment for the patient". - Lead nurse

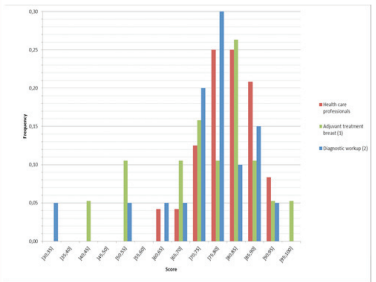
"This demands that the physician uses it 100 % - that we turn everything around and say; "We want this" - Physician

"I like that this will induce that I will be asked what matters to me – if the physician uses it correctly". -Patient

"I like that this will turn off the "record player" from the physician, so he does not forget, that a human being is sitting in front of him". -Patient

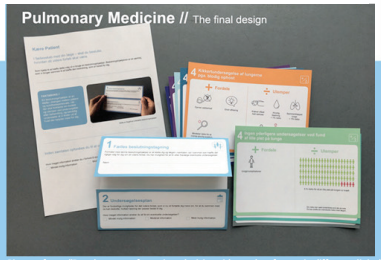
"This means I am more aware of risks from diagnostic examinations. It has the effect that I will consider risks much more". -Patient

RESULTS



Preparation for Decision Making, score converted to 0-100 scale. Statistical test showed that there was no significant difference in the distributions of the scores by patients and relatives in the two demonstration projects. In both projects scores were generally good, and showed that the PtDA template were useful in both of the chosen clinical decision making situations.

PtDA's



Pictures from: "Development of a patient decision aid template for use in different clinical settings", accepted for publication in *European Journal for Person Centered Healthcare*

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Steffensen KD[1,2,3], Fokdal LU[4], Oer Knudsen A[5], Vestergaard Madsen C[2], Jensen PT[6,7], Lundvall L[8], Olling K[1], Lemley B[9], Blou D[9], Büchmann H[9], Haee M[4]

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Danish Cancer Research Days
Aug. 30.-31., 2018

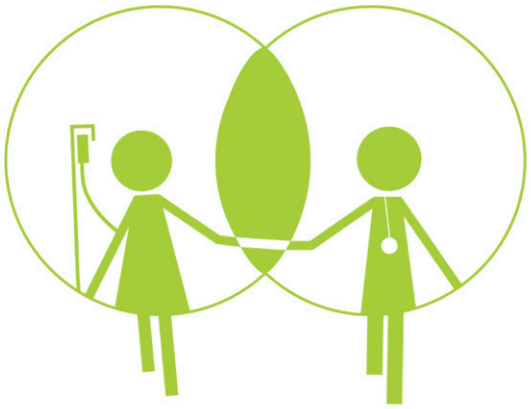
Shared decision making in care for the gynecologic cancer patient

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. There is compelling evidence that patients who are active participants in the management of their health care have better outcomes, than patients who are passive recipients of care.

Shared decision making (SDM) is a collaborative process between patient and clinician when decisions are to be made about diagnosis, treatment or follow-up in order to ascertain which options are preferable to the patient. This includes use of evidence-based information concerning options, benefits, harms, uncertainties and medical counselling and support to explore the patient's own values and preferences.

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

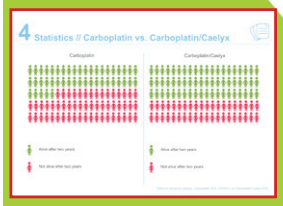


CONCLUSION

The decision aid is part of a Shared Decision Making package, which will support a paradigm shift and implementation of SDM in clinical practice.

The project is ongoing and future work includes testing and implementation of the DA in clinical setting.

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 PtDA template is easy to adjust and is also applicable when developing new PtDA's for other clinical decisions within Danish healthcare.



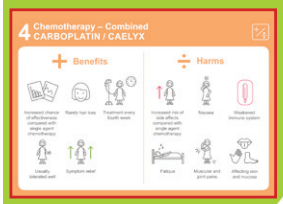


Fig 2. Using pictograms the cards presents the pros and cons of the various treatment options. One card per option making the patient able to compare potential benefits and harms side by side. In addition, there are cards of authentic stories from other patients who have experienced a similar choice, as well as cards with e.g. timelines and statistics, all of which support the patient in the decision process.

MATERIALS

Development, testing, evaluation, and implementation of a PtDA for women with relapsed ovarian cancer will be performed at three hospitals in Denmark. The research group includes three patient representatives with ovarian cancer along with doctors and nurses from the above-mentioned hospitals, representatives from the Danish Cancer Society and a representative from Center for Shared Decision Making.

Center for Shared Decision Making has, in collaboration with clinicians, patients, relatives, international researchers and designers, developed a Danish generic platform that can be used as a general template for developing and building a PtDA for a specific clinical decision (Fig 1).
The platform has been tested in various clinical settings. The development of the platform has followed existing quality guidelines and complies with the parameters set forth in International Patient Decision Aid Standards (IPDAS) Collaboration. This PtDA generic template will be used to develop two new PtDA's for patients with recurrent ovarian cancer.

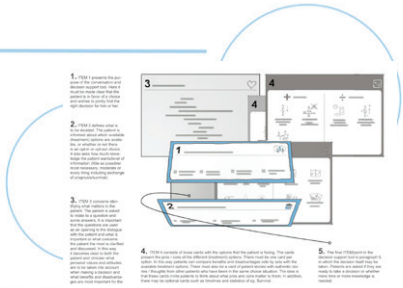


Fig 1. An illustration of the patient decision aid template and the five essential items included in it. Steffensen KD, Vinter M, Crüger D, Dankl K, Coulter A, Stuart B, Berry LL. Lessons in integrating Shared Decision-Making Into Cancer Care. *J Oncol Pract*. 2018 Apr;14(4):229-235

METHODS

At relapse the treatment options depends on the platinum-free interval. Based on the existing generic PtDA platform, we have developed a PtDA for both platinum-sensitive and platinum-resistant disease. During the development of the PtDA, focus has been on patient involvement, as well as systematic literature review, discussion of evidence, endpoints, survival and side effects. The tests of the two PtDA's will take place at Aarhus University Hospital, Odense University Hospital and Vejle Hospital, where the two PtDA's will be tested by both patients and clinicians.

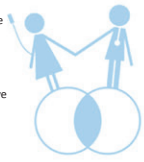
After the development of the two PtDA's for treatment options and shared decision making for patients with recurrent ovarian cancer, the next step of the project will be a two-step test phase:

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) Beta test: 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 PtDA (Beta test 1) and after the use of the PtDA (Beta test 2).

RESULTS

Based on the existing generic platform we have developed two PtDA's – one for platinum-sensitive and one for platinum-resistant relapse (Fig 2).



The PtDA's were developed in a paper version, as patients who have been involved in the development phase, have expressed their wish for this compared to a digital decision aid. It consists of a folder wrapped around a number of insertable cards. Each card describes the treatment options and potential harms and benefits to be discussed with the patient during a consultation.

The patient-clinician conversation in which the PtDA is used consists of 5 steps:

1. The purpose of the PDA is presented.
2. The patient is informed of the available treatment options.
3. The patients personal preferences are identified; what is important/concerns the patient.
4. Patient's options and harms/benefits of each option are reviewed (on the insertable cards).
5. A shared treatment decision is made between clinician and patient.

PROs in lung cancer: Experiences from a Danish feasibility study

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Background

The objective of this study was to introduce a method for collecting patient reported outcomes (PROs) nationwide in a lung cancer population. By incorporating these outcomes in a national database, we want to assess the possibilities of using PROs as a measure of quality in the treatment of lung cancer.

Methods

All patients who were registered with a histologically verified lung cancer in the Danish Lung Cancer Registry (DLCR) during a 2-year period (from 1 October 2013 until 30 September 2015) were included in the project. For collection of PROs, we used the Danish versions of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 ("Quality of Life Questionnaire Core 30") and EORTC QLQ-LC13 ("Quality of Life Questionnaire Lung Cancer 13"). During the first year after diagnosis, the patients were asked to fill out questionnaires four times. The first questionnaire (QoL_0) was handed out in the hospital departments before treatment. The next three (QoL_{1-3}) were mailed to the patients systematically, after a check that the patient was still alive, at 3 months, 6 months and 12 months after initiation of first treatment. All questionnaires returned were incorporated in DLCR.

Results

Of 7,258 lung cancer patients eligible for inclusion, at least one questionnaire was completed by 4,443 patients. Of these, 2,592 completed two and 1,414 completed three questionnaires. Patient characteristics for responders and non-responders are shown in table 1.

Table 1: Patient characteristics

Table 1	Patients with ≥ 1 questionnaire		Non-responders		Responders vs. Non-resp.
	Nresp = 4,443	%	Nnonr = 2,815	%	p-value
Sex					0.016
Male	2,165	48.7	1,453	51.6	
Female	2,278	51.3	1,362	48.4	
Age					0.008
Median	69		69		
Range	17 -96		23-93		
Stage					< 0.001
IA	780	17.6	206	7.3	
IB	431	9.7	109	3.9	
IIA	211	4.8	67	2.4	
IIB	216	4.9	113	4.0	
IIIA	524	11.8	269	9.6	
IIIB	459	10.3	254	9.0	
IV	1,614	36.3	1,636	58.1	
Not reported	208	4.7	161	5.7	
Cell type					< 0.001
Small cell	634	14.3	497	17.7	
Squamous	873	19.7	542	19.3	
Adeno	2,006	45.2	1,081	38.4	
Other	930	20.9	695	24.7	
Initial treatment					< 0.001
Resection	1,373	30.9	332	11.8	
Curative oncology	1,138	25.6	429	15.2	
Palliative oncology (incl. NA)	1,932	43.5	2,054	73.0	
Performance status (score)					< 0.001
Normal activity (0)	2,134	48.0	824	29.3	
Symptoms (1)	1,366	30.7	846	30.1	
Sometimes in bed (2)	397	8.9	460	16.3	
Mostly in bed or chair (3)	110	2.5	273	9.7	
Confined to bed or chair (4)	17	0.4	50	1.8	
Not reported	419	9.4	362	12.9	
Lung function (median)					< 0.001
FEV1 - % of expected value	73.5		66.7		
Not reported	740	16.7	653	23.2	
Charlson Comorbidity Index					0.153
0	2,115	47.6	1,291	45.9	
1	968	21.8	602	21.4	
≥2	1,360	30.6	922	32.8	

Response rates divided in four 6-month periods are shown in table 2. Response rate means for QoL_{1-3}, were 43.6%, 57.7% and 49.2%, respectively.

Table 2: Response rates

Table 2	TOTAL	1.10.13 - 31.3.14	%	1.4.14 - 30.9.14	%	1.10.14 - 31.3.15	%	1.4.15 - 30.9.15	%
New patients in DLCR	9,394	2,345		2,334		2,400		2,315	
Patients included	7,258	1,831		1,811		1,850		1,766	
Inclusion %	77.3	78.1		77.6		77.1		76.3	
QoL0	1,210	356		332		281		241	
QoL0, Exit	23	11		7		3		2	
Qualified* QoL1	6,074	1,533		1,526		1,525		1,490	
QoL1	2,777	707	**46.1**	390	**25.6**	691	**45.3**	856	**57.5**
QoL1, Exit		0		0		8		4	
Exit1		298		285		325		276	
Qualified* QoL2	5,173	1,304		1,282		1,303		1,284	
QoL2		727	**55.8**	708	**55.2**	760	**58.3**	778	**60.6**
QoL2, Exit		10		10		7		0	
Exit2 cumulative	2,085	527		529		547		482	
Qualified* QoL3	3,867	962		955		980		970	
QoL3		474	**49.3**	500	**52.4**	507	**51.7**	414	**42.7**
QoL3, Exit		4		3		3		3	
Exit3 cumulative	3,391	869		856		870		796	
Returned in total	8,722	2,264		1,930		2,239		2,289	

Included: Patients treated for histologically verified lung cancer
*Qualified means alive after 3, 6 and 12 months, respectively
Exit includes patients that have died at 3, 6 and 12 months (90, 180 and 360 days)
QoLx, Exit are patients that did fill out a questionnaire, but died at 3, 6 and 12 months

Conclusion

Despite the severe morbidity and extremely high mortality rate in lung cancer, it was possible to achieve response rates after treatment close to 50 or even 60% in a lung cancer population. To increase response rates *before* treatment further, questionnaires should be delivered to the patients more systematically.

If this effort to increase response rates before treatment will succeed, and acceptable response rates both before and after treatment is achieved, it might be possible to use PROs as a measure of quality in the treatment of lung cancer.

Systematic Review of the Impact of Socioeconomic, Demographic and Religious Factors on Quality of Life in Ostomized Colorectal Cancer Survivors

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Methods

Pubmed+Embase+CINAHL+PSYCInfo
- Cohort of ostomized CRC survivors
- > 6 months follow up
- Validated HRQoL instrument
- Demographic, socioeconomic or religious factors
- Peer reviewed publication
- English language

738 studies screened
6 studies included

Most studies were...
Small (n< 100)
Cross-sectional
Exploratory

Results

Gender
5 studies, lower HRQoL in females:

↓ physical wellbeing
↓ general health
↓ mental health
↓ body image
↑ GI-symptoms

Age
3 studies, no age-effect
2 studies, lower HRQoL in the young
↓ physical function
↓ social function
↓ body image
↑ sexual problems

Income
Education
Employment
3 studies found no correlation to HRQoL

Religion
1 study found no correlation to HRQoL

Conclusions

Conclusions
- Females experience lower HRQoL compared to males
- Younger ostomates experience more negative impact on HRQoL than older
- Ostomates experience a financial burden, but a correlation to socioeconomic status was not found
- No conclusions can be drawn on religious factors' impact on HRQoL

But why...
- do females fare worse?
- do the elderly cope better?
- does income not correlate even when ostomates experience a financial burden?

And...
- do the questionnaires really capture all stoma-related problems affecting HRQoL?
- we need to know more!

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Elevated mean fractional exhaled nitric oxide and radiation pneumonitis in patients with non-small cell lung cancer

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Introduction

Radiation pneumonitis (RP) is a potentially fatal side effect of thoracic high-dose radiation therapy (HDRT). Prediction of symptomatic RP is challenging and clinically useful markers are lacking. The fractional exhaled nitric oxide (FeNO) was observed elevated in small group of patients with symptomatic RP after HDRT for oesophageal and lung cancer.

The aim of the study

To investigate the correlation between the grade of symptomatic RP and the mean FeNO during and after HDRT in patients with non-small cell lung cancer (NSCLC).

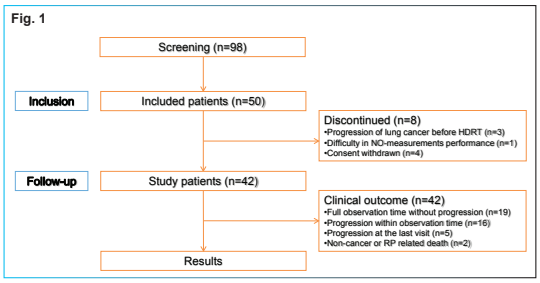
Materials & Methods

50 patients with NSCLC referred to HDRT of a total dose of 60-66 Gray (Gy) in 2 Gy per fraction between 2012 – 2016 (Fig. 1).

- FeNO was measured on NIOX MINO® and VERO® (Aerocrine, Solna, Sweden) 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.
- Toxicity was described using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.
- Statistical analyses included demographics, dosimetric factors, pulmonary function tests (PFTs) and mean FeNO differences.

The project was approved by the Ethics Committee of North Jutland (NO-20120029) and reported to the Data Protection Agency (2008-58-0028).

Fig. 1



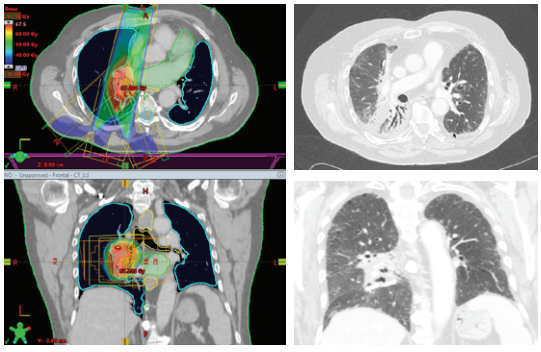
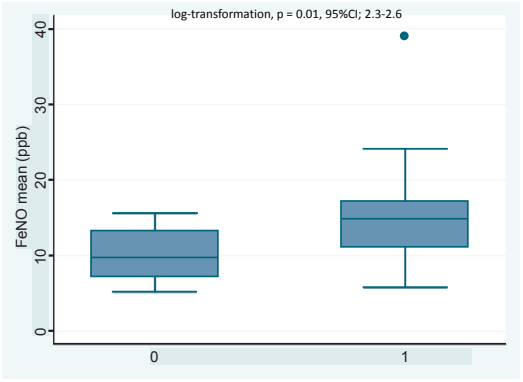


Fig. 2 Dose wash on CT simulation scan and corresponding CTCAE grade 3 RP

Fig. 3



CTCAE grade < 2 RP

Mean FeNO = 10.3 ppb
(95%CI; 8.6 - 11.9, SD 3.4)

CTCAE grade ≥ 2 RP

Mean FeNO = 15.0 ppb
(95%CI; 12.0–18.0, SD 7.1)

Results

Data of 42 patients, that completed HDRT.

- RP of CTCAE grade ≥ 2 was observed in 24 out of 42 patients (Fig. 2).
- RP occurred on average 81 (3 – 166) days after HDRT.
- The difference in mean FeNO between the groups was significant (log-transformation, p = 0.01, 95%CI; 2.3-2.6) (Fig. 3).
- After adjustment for smoking and steroid treatment, the difference of the mean FeNO between patients with and without RP was no longer significant (p = 0.09, 95%CI; 0.78-26.1).
- Chronic obstructive pulmonary disease (COPD) was observed equally in both groups (p = 0.86) without any difference between forced expiratory volume in 1 second (FEV1) at baseline (p = 0.18) and after HDRT (p = 0.18) within and between the groups.
- Dosimetric quantities as mean lung dose and the lung volume receiving > 5, 20, 40, 50 and 60 Gy respectively (V5, V20, V40, V50 and V60) was not statistically significant between patients with and without RP.

Conclusions

The mean value of FeNO in patients with CTCAE grade ≥ 2 RP after HDRT for NSCLC was significantly higher than in patients without RP. Smoking and peroral steroid treatment reduce the predictive power of the mean FeNO. Neither PFTs nor dosimetric parameters were predictive for symptomatic RP.

Future plan

Machine learning method is planned to be used in the future to design a mathematical predictive model for CTCAE grade ≥ 2 RP combining FeNO, dosimetric parameters and clinical data.

AALBORG UNIVERSITY HOSPITAL

REGION

Patient- and observer-reported long-term scar quality of wide local excision scars in melanoma patients

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INTRODUCTION

The incidence of melanoma is unfortunately increasing, particularly in countries with predominantly Caucasian populations. Fortunately, the survival rates are also increasing due to earlier detection of the primary tumour and treatment improvements. Wide local excision (WLE) of the primary tumour is the mainstay of treatment for melanoma patients.

AIM

The aims of this study were 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 the POSAS, and to identify factors influencing the scar assessment.

METHOD

In this cross-sectional study, we included patients who were treated for cutaneous melanoma stage I-III between 1997 and 2015 at our department. Inclusion criteria were primary tumour located on the trunk or limbs, with the defects closed either directly or with the use of a local flap. Exclusion criteria were primary tumour location on the hands or feet, and WLE scars not assessed by the patients because of location on a non-visible site of the body.
The POSAS which consists of a patient (PSAS) and a observer (OSAS) sub-scale was used to evaluate the WLE scars. Both the PSAS and OSAS consist of two scales: A six-item "total score" scale and a single-item "overall opinion" scale. The sub-items are scored numerically on a 10-point scale with 1 representing normal skin and 10 representing that the outcome is very different from normal skin, giving a "total score" range of 6 to 60 and an "overall opinion" range of 1 to 10 (Figure 1).

The patients filled in the PSAS prior to a clinical evaluation of the WLE scar performed by a single observer (last author), who filled in the OSAS and additional items on unfavourable scar characteristics (e.g. keloids and suture marks).
The observer was blinded to the patients' assessments.
Descriptive statistics were used to describe the study population and WLE scars.

The internal consistency, convergent validity, and inter-rater reliability of the POSAS was examined with Spearman's rho (r_s)* and Cronbach's alpha (α)*, respectively. Factors (POSAS sub-items and additional factors) influencing the patient- and observer-reported scar quality were tested in regression analyses

RESULTS

Data regarding the 320 patients included is shown in table 1. The overall opinion score was moderate in both the PSAS (*M*= 4, *SD*= 3) and OSAS (M= 4, *SD*= 2).
The internal consistency, evaluating the correlation of the sub-items was good in both the PSAS (α= 0,85) and OSAS (α= 0,70). The convergent validity, evaluating the correlation of the total score and the overall opinion score was strong in both the PSAS (r_s= 0,83, p >0,0001) and OSAS (r_s= 0,81, p >0,0001) . The inter-rater reliability, evaluating the correlation of the PSAS and OSAS overall opinion, was only moderate (r_s= 0,39, p >0,0001) (Figure 2).
The patients were influenced by the PSAS sub-items: colour, irregularity, thickness and pain. The observer was influenced by the OSAS sub-items: vascularity, surface area, thickness, relief and pliability (Table 2).
Both patient- and observer-reported scar qualities were influenced by age, location, type of superficial suture, keloids and widened scars.
Moreover, the patients were influenced by the scar tightness and the observer was influenced by postoperative complications, hypertrophic scars, suture marks and dog ears (Table 3).

CONCLUSION

The study is unique as it is the first of its kind covering the patient- and observer-reported long-term scar quality after WLE in Danish melanoma patients.
In general, the WLE scar quality was good. However, discrepancy was found between the patient- and observer-reported scar quality and the factors influencing patient- and observer-reported scar quality differed. A better understanding of this may improve treatment and hence patient-reported scar quality.
Additionally, we found the POSAS to be a reliable and valid scar assessment tool.

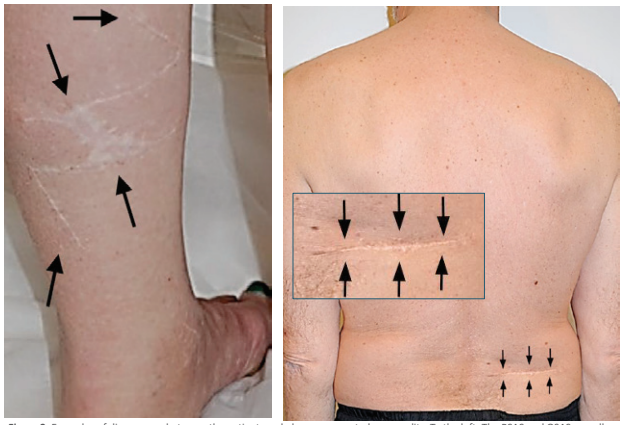

Figure 2. Examples of discrepancy between the patient- and observer-reported scar quality. To the left: The PSAS and OSAS overall score was 2 and 8, respectively. To the right: The PSAS and OSAS overall score was 10 and 2, respectively (Range 1–10; 1=as normal skin, 10=very different from normal skin).

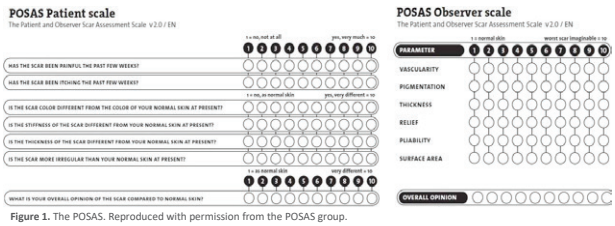

Figure 1. The POSAS. Reproduced with permission from the POSAS group.

Table 1. Patient, treatment, and scar characteristics.

Patient data	No (%) or mean (SD), range
Ethnicity	
Caucasian	318 (99%)
Other	2 (1%)
Age at time of study (years)	57 (12), 22-76
Gender	
Male	153 (48%)
Female	167 (52%)
BMI (kg/m²)	27 (4), 16-47
Low weight (BMI <20)	4 (1%)
Normal weight (BMI 20-25)	117 (37%)
Overweight (BMI >25)	199 (62%)
Smoker at the time of surgery	45 (14%)
Time since surgery (years)	5 (3), 1-16
Scar location	
Back	69 (22%)
Chest/abdomen	82 (26%)
Arm	58 (18%)
Leg	111 (35%)
Excision margins	
< 2 cm	65 (20%)
≥ 2 cm	255 (80%)
Type of closure	
Direct	254 (79%)
Local flap	66 (21%)
Type of superficial suture	
Interrupted/running non-absorbable	141 (44%)
Intradermal non-absorbable	123 (38%)
Intradermal absorbable	56 (18%)
Postoperative complications*	62 (19%)
Unfavourable scar characteristics	
Hypertrophic	14 (4%)
Keloid	18 (6%)
Widened	149 (47%)
Depressed	4 (1%)
Suture marks	129 (40%)
Dog ears	71 (22%)
Self-reported tightness of scar	
No	221 (69%)
Yes	99 (31%)
Affecting range of movement, if tightness of scar (n=99)	
No	72 (73%)
Yes	27 (27%)

SD: Standard deviation, BMI: Body Mass Index, *<30 days postoperative; hematoma, seroma, wound infection, dehiscence.

Table 2. Multivariable linear regression analyses of the correlation between the PSAS and OSAS sub-items and overall opinion of the WLE scar.

PSAS			
Variables	β	95% CI	*p*-value
Colour	0.25	0.16;0.34	<0.001
Irregularity	0.55	0.45;0.65	<0.001
Thickness	0.18	0.04;0.32	0.01
Pain	0.21	0.07;0.35	0.004
Stiffness	-0.07	-0.20;0.05	0.25
Itching	-0.04	-0.17;0.09	0.56
OSAS			
Variables	β	95% CI	*p*-value
Vascularity	0.14	0.08;0.21	<0.001
Surface area	0.54	0.43;0.65	<0.001
Thickness	0.29	0.18;0.40	<0.001
Relief	0.20	0.10;0.30	<0.001
Pliability	0.61	0.26;0.96	<0.001
Pigmentation	0.03	-0.08;0.13	0.63

β: Correlation coefficient, CI: Confidence interval.

Table 3. Multivariable linear regression analyses of the correlation between the patient, treatment and scar variables and the PSAS and OSAS overall opinion of the WLE scar, respectively.

PSAS			
Variables	β	95% CI	*p*-value
Age at time of study	-0.06	-0.09; -0.03	<0.001
Gender			
Female	0 (ref.)	0 (ref.)	0 (ref.)
Male	-0.42	-1.06; 0.23	0.21
BMI (kg/m²)	0.01	-0.06;0.08	0.71
Smoker at the time of surgery	-0.10	-0.94; 0.74	0.81
Scar location			
Back	0 (ref.)	0 (ref.)	0 (ref.)
Chest/abdomen	-1.00	-1.84; -0.17	0.02
Arm	-0.61	-1.55; 0.32	0.19
Leg	-1.52	-2.35; -0.69	<0.001
Excision margin			
< 2 cm	0 (ref.)	0 (ref.)	0 (ref.)
≥ 2 cm	0.42	-0.34; 1.17	0.28
Type of closure			
Direct closure	0 (ref.)	0 (ref.)	0 (ref.)
Local flap	-0.03	-0.80; 0.75	0.95
Type of superficial suture			
Interrupted/running non-absorbable	0 (ref.)	0 (ref.)	0 (ref.)
Intradermal non-absorbable	-0.88	-1.54; -0.22	0.01
Intradermal absorbable	-0.76	-1.64; 0.12	0.09
Time since surgery	0.02	-0.07; 0.11	0.69
Postoperative complications	0.53	-0.25; 1.31	0.18
Unfavourable scar characteristics			
Hypertrophic	0.41	-0.99; 1.81	0.57
Keloid	2.42	1.17; 3.67	<0.001
Widened	0.60	0.00; 1.20	0.049
Depressed	2.29	-0.30; 4.88	0.08
Suture marks	0.02	-0.60; 0.65	0.95
Dog ears	0.49	-0.23; 1.21	0.18
Patient-reported tightness of scar	1.43	0.91; 1.94	<0.001
Affected range of movement because of tightness of scar	-0.5	-0.93; 0.82	0.90

OSAS			
Variables	β	95% CI	*p*-value
Age at time of study	-0.02	-0.3; -0.00	0.03
Gender			
Female	0 (ref.)	0 (ref.)	0 (ref.)
Male	0.16	-0.19; 0.52	0.37
BMI (kg/m²)	0.01	-0.03; 0.05	0.53
Smoker at the time of surgery	-0.23	-68; 0.23	0.33
Scar location			
Back	0 (ref.)	0 ref.)	0 (ref.)
Chest/abdomen	-0.35	-0.82; 0.11	0.14
Arm	-0.18	-0.70; 0.33	0.49
Leg	-0.62	-1.08; -0.16	0.01
Excision margin			
< 2 cm	0 (ref.)	0 (ref.)	0 (ref.)
≥ 2 cm	0.36	-0.06; 0.78	0.09
Type of closure			
Direct closure	0 (ref.)	0 (ref.)	0 (ref.)
Local flap	-0.17	-0.60; 0.26	0.43
Type of superficial suture			
Interrupted/running non-absorbable	0 (ref.)	0 (ref.)	0 (ref.)
Intradermal non-absorbable	-0.41	-0.78; -0.04	0.03
Intradermal absorbable	-0.68	-1.17; -0.19	0.01
Time since surgery	0.02	-0.03; 0.07	0.41
Postoperative complications	0.52	0.09; 0.95	0.02
Unfavourable scar characteristics			
Hypertrophic	1.03	0.25; 1.81	0.01
Keloid	2.98	2.29;3.67	<0.001
Widened	0.72	0.38; 1.05	<0.001
Depressed	1.18	-0.26; 2.62	0.11
Suture marks	0.63	0.28; 0.97	<0.001
Dog ears	0.55	0.15; 0.95	0.01

Ref.: reference, BMI: Body Mass Index, β: Correlation coefficient, CI: Confidence interval.

*Spearman's rho (r_s) ranges from -1 to 1 and Cronbach's alpha (α) range from 0 to 1. r_s ≥0.7 indicate strong correlation. α ≥0.7 indicate acceptable consistency.

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Implementering af synkestrukturer som risikoorganer i DAHANCAs stråleretningslinjer

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Introduktion

Danmark har haft nationale retningslinjer for strålebehandling af hoved- og halskræft (HN) siden 1990 [1]. Retningslinjerne bliver jævnligt opdaterede og er netop under revision (2017/2018). En væsentlig ændring bliver at flere synkeorganer inkluderes i DAHANCAs dosisgrænsetabel. Formålet med indeværende undersøgelse, var at lade de 6 HN-stråleterapicentre i DK individuelt inkludere synkeorganerne i beregningen af en teststrålebehandling. En efterfølgende workshop skulle sikre fælles forståelse og bevidsthed omkring muligheden for at øge kvaliteten af stråledosisplaner for at begrænse patienternes bivirkninger efter strålebehandling.

Resultater og Konklusion

Alle targets modtog tilstrækkelig dosis og alle kritiske organer, såsom rygmarv og hjernestamme, blev skånet tilstrækkeligt i alle dosisplaner. For synkerelaterede organer i svælget blev der imidlertid observeret store variationer med standardafvigelser (SD) på op til 7 Gy fra middelværdien (konstriktor muskel nedre svælg, PCM) svarende til en dosisforskel på 16 Gy mellem den laveste (29 Gy) og den højeste (45 Gy) dosis til organet, se figur 1 (blå). Fig. 1 viser også resultaterne for den kontralaterale (venstre) ørespytkirtel (parotis, rød). Andre organer med store forskelle i opnået skånegrad var glottisk (SD = 6 Gy) og supraglottisk (SD = 5 Gy) strubehoved, se oversigt i tabel 1. Generelt blev størstedelen af dosisgrænserne for risikoorganerne overholdt. De store variationer i opnåede gennemsnitlige doser til synkeorganerne indikerer et behov for supplerende træning, erfaringsudveksling og flere nationale workshops for at forbedre og ensrette behandlingskvaliteten.

OAR / Center	1	2	3	4	5	6	Mean [Gy]	SD [Gy]	Guide-lines [Gy]
PCM_low	35	41	45	29	44	45	40	6.6	55
PCM_Mid	50	49	56	44	54	54	51	4.3	55
PCM_Up	32	34	35	30	34	34	33	2.0	55
Larynx_SG	36	38	39	30	37	46	38	5.1	40
Larynx_G	31	35	39	30	36	44	35	5.5	40
BucMuc_L	22	21	18	17	22	29	21	4.3	35
BucMuc_R	31	25	29	18	29	36	28	5.8	35
OralCavity	28	26	23	25	29	31	27	2.7	30
Esophagus	13	18	11	11	19	17	15	3.4	40
Parotid_L	19	20	15	16	18	22	18	2.5	26
Parotid_R	25	24	26	19	25	30	25	3.5	26
Subm_L	37	35	33	30	35	40	35	3.4	35
Subm_R	55	50	57	56	57	53	55	2.8	35

Tabel 1: Middeldoser til synkeorganerne for center 1-6 samt middelværdi af planlægningsresultaterne, SD og dosisgrænser fra nye retningslinjer. Risikoorganer skrevet med rødt, introduceres i 2018-versionen af retningslinjerne. Her opdeles strubehovedet også i to dele (supraglottisk og glottisk del).

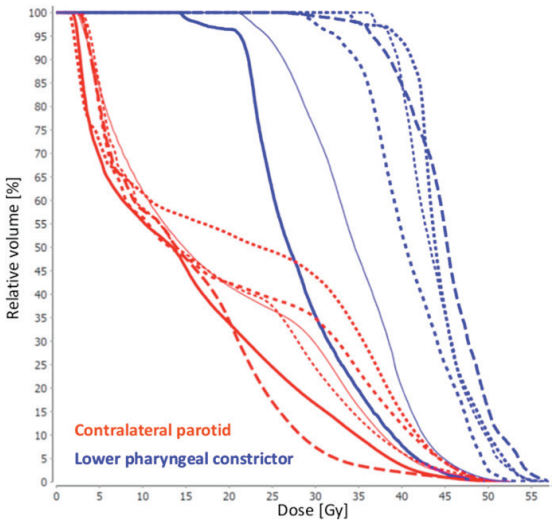
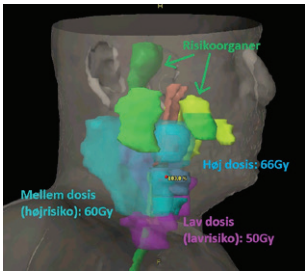


Fig. 1. Dosis-volumen histogrammer for nedre svælgs konstriktor (blå) og kontralaterale ørespytkirtel for de 6 centre.

Methods

De seks danske centre, som strålebehandler hoved- og halskræft deltog alle i undersøgelsen og den efterfølgende workshop. En anonymiseret CT-scanning fra en patient med forhåndsindtegnede sygdomsområder og risikoorganer blev sendt til centrene. Patienten havde kræft i mundsvælget, og den foreskrevne dosis var 66 Gy/33 fraktioner til højdosisområder, 60 Gy til det højrisiko elektive område og 50 Gy til lavrisiko elektive områder. Hvert center udarbejdede en dosisplan i henhold til de reviderede (2018) retningslinjer. Dosisplanerne blev sammenlignet og evalueret på en national workshop med særlig opmærksomhed på følgende synkeorganer: Svælgets konstriktormuskulatur, strubehoved, mundhule, kindslimhinder, spiserør, ørespytkirtler og kæbespytkirtler. Planlægningsteknikkerne varierede over centrene. Det enkelte centers erfaring med optimering af doser i henhold til de nye synkeorganer (tabel 1, rød tekst) varierede fra nul til adskillige måneder. Synkeorganerne blev ikke prioriteret i forhold til hinanden.



Reference: [1] DAHANCAs stråleretningslinjer kan downloades fra: https://www.dahanca.oncology.dk

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PROTON-STRÅLEBEHANDLING AF KRÆFT I NÆSE OG BIHULER. ET DAHANCA STUDIE.

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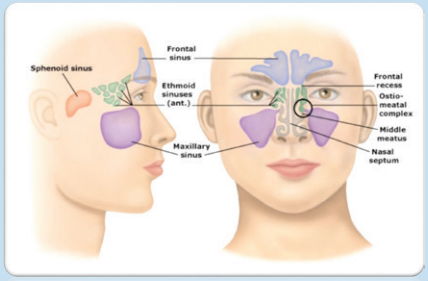
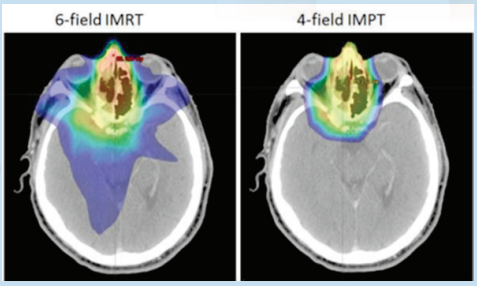
Baggrund

- Kræft i næse/bihuler er ofte vokset ind i de omgivende væv på diagnosetidspunktet.
- Behandles ofte med både kirurgi og stråleterapi.
- Næse-bihule kræft er svært at behandle, på grund af knudernes beliggenhed nær ved hjerne og øjne/synsbaner.
- Bestråling af hjerne og øjne/synsbaner kan resultere i senfølger der har stor betydning for patienternes livskvalitet.



Proton terapi

- Protonterapi er en mere skånsom form for strålebehandling.
- Dette bliver en mulighed i Danmark når Dansk Center for Partikelterapi åbner i 2019.
- Vi håber at kunne reducere bivirkningerne og øge livskvaliteten for patienterne med protonterapi.
- Der er fortsat fysiske usikkerheder ved proton terapi, som gør det svært at forudse effekten.



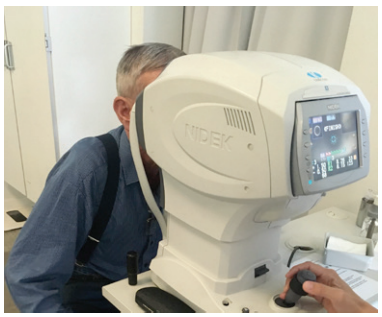
Behandlingsplan til den samme patient med hhv. røntgenstråler og protoner, illustrerende den reducerede samlede dosis.
The Danish National Particle Center, 2011.

De Store Spørgsmål

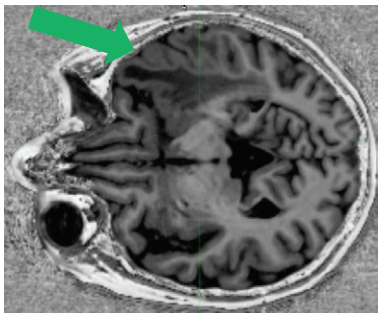
Kan vi reducere påvirkningen af øjnene og synsbanerne?

Kan vi reducere påvirkningen af hjernen?

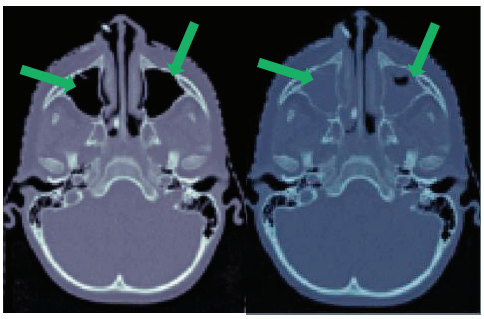
Kan vi levere en behandling der er sikker og præcis?



Øjenundersøgelse af patient der tidligere er strålebehandlet for næse-bihulekræft med henblik på at afklare om patienten har senfølger fra øjne eller synsapparat.
AUH, 2018



MR-scanning af patient der tidligere er behandlet for næse-bihulekræft. Man ser ændret struktur i hjernevævet i patientens højre side (pil) svarende til det område der er udsat for bestråling.
AUH, 2018



CT scanning af den samme patient på to forskellige tidspunkter i et strålebehandlingsforløb. Der er stor forskel på luft-væske sammensætningen i kæbehulerne (pile), og det kan have stor indflydelse på hvor præcist strålerne kan ramme.
Phys. Med. Biol. ***63*** *(2018) 025020*

DANSK CENTER FOR PARTIKELTERAPI

Organisatorisk brugerinddragelse i udvikling af forskningsbaseret patientinformation om protonterapi

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Baggrund

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.

Konklusion

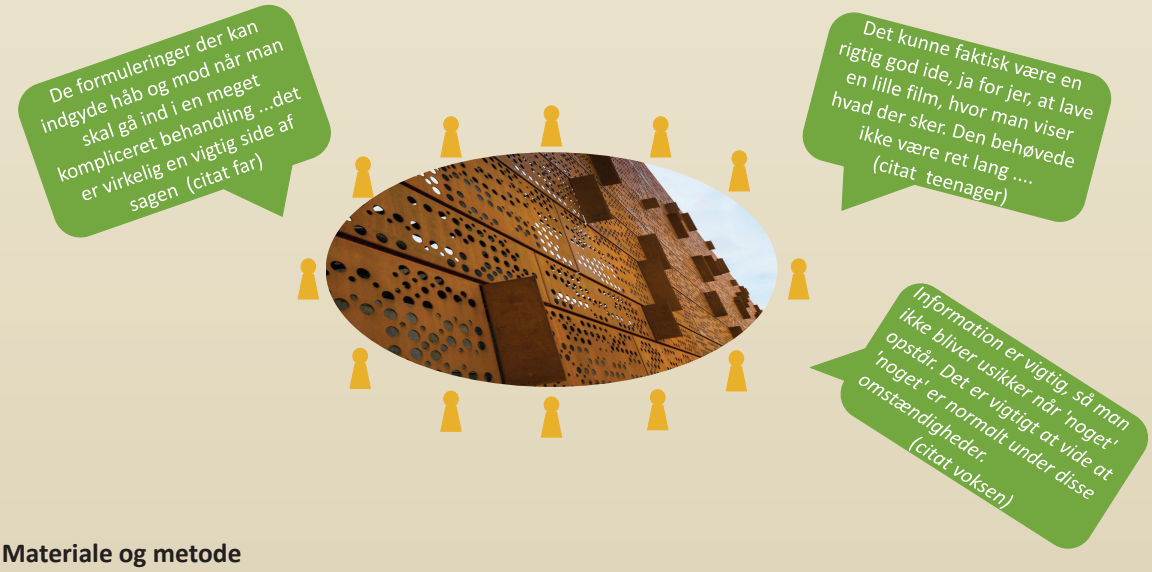
Den benyttede metode til organisatorisk brugerinddragelse har vist sig anvendelig til at repræsentere patientperspektivet ved udarbejdelse af forskningsbaseret patientinformation i DCPT.

Resultater

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).



Materiale og metode

Kvalitative semi-strukturede 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 blev gennemlyttet af to personer individuelt og meningskondenseret ud fra en Ricoeur inspireret analysemodel. Dette blev sammenholdt og man opnåede enighed om definition af nye temaer.
Den forskningsbaserede patientinformation kvalitetssikres ved et brugerpanel bestående af interviewpersonerne. Herved sikres genkendelighed mellem patienternes udtalelser og det færdige produkt.

Danske Kræftforskningsdage 2018

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#78

"See and treat" in an outpatient setting in women age ≥ 45 years with cervical dysplasia

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Background

In Denmark, 370 women are diagnosed with cervical cancer every year.
Older women are more likely to be diagnosed with advanced stage disease and have a higher mortality compared to younger women.
Examinations of postmenopausal women for cervical dysplasia is a challenge due to:

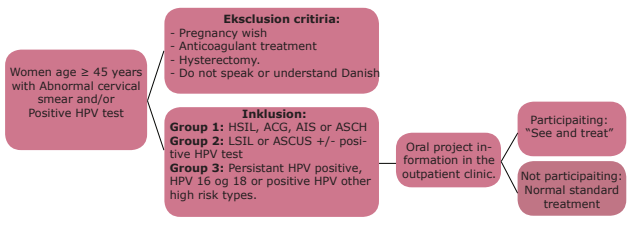
- Decreased sensitivity of cervical cytology in older women
- Low performance of colposcopy due to retraction of the transformation zone
- Multiple visits at the outpatient clinic are usually required

Methods

Women age ≥ 45 years referred to the Departments of Obstetrics and Gynecology in Central Denmark Region due to abnormal cervical cytology result or positive HPV test from August 2018 to August 2022 will be included in the study.
We expect to include approximately 150 women.
"See and treat" is a combined procedure with:

- Cervical cytology and HPV test
- Colposcopy and cervikcal punch biopsies
- Loop electrosurgical excisional procedure

Figure 1: Referral and inclusion of the patients.



Aim

To investigate if the implementation of "see and treat":

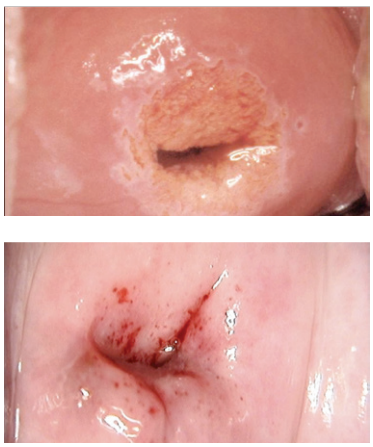
- Can optimize the diagnostics of cervical neoplasia
- Can improve the clinical follow-up and treatment

Perspective

Our results may provide;

- Evidence-based treatment of high-risk HPV-positive women and women with abnormal cervical cytology
- A estimate of the prevalence of cervical intraepithelial neoplasia in our cohort
- Provide knowledge on patient experience and satisfaction
- A cost-effective evaluation of "see and treat"
- To reduce cervical cancer incidence and mortality in the long run

Figure 2: Premenopausal cervix with visible transformation zone and postmenopausal cervix with retraction of the transformation zone.



#79

Perceptions of subsequent screening after a false alarm for colorectal cancer

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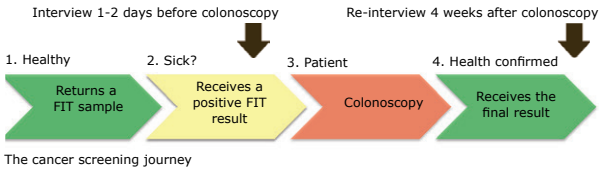
Background

- Colorectal cancer screening can reduce colorectal cancer incidence and mortality
- The Danish colorectal cancer screening program offers home-based fecal immunichemical testing (FIT).
- Participation rate: 61%. Positive FIT rate: 7%. Follow-up colonoscopy attendance: 90%
- Colorectal cancer diagnosis: 6%
- "False alarm" for colorectal cancer: no abnormalities: 45%; polyps/adenomas: 55%.
- No long-term negative psychological impact on screening participants
- Coping before follow-up colonoscopy?
- Attitudes to screening after a "false alarm" for cancer?

Aim

- to explore how participants in a colorectal cancer screening program perceive and manage a positive screening result, followed by a non-cancer colonoscopy result.



The cancer screening journey

Methods

- Recruitment: screening administration call center
- Maximum variation sampling: age, sex, marital status
- Interviews in participants' own homes
- Interviews before and after colonoscopy: 45-90 minutes
- Transcriptions, field notes: thematic analysis, ethnography

Results

Themes before colonoscopy:
- Symptom appraisal: Hemorrhoids? Polyps? (Cancer?)
- Communication strategies: discuss with family/friends? Keep to oneself? (Contact healthcare professional?)

Themes after colonoscopy:
- Trust in medical skills, confidence in negative result (no cancer)
- Patient involvement (no or little sedation), relief, gratitude
- Obligation to participate in screening – individual, social, towards society

Man, 58, single: I'm sure it's just the stupid hemorrhoids. And I think it's okay just to get it checked, because then it's done, and if it's not okay, I better do something about it.

Man, 58, married: I have two children in their late twenties and there is no reason to upset them, so they don't know that I am going to get an examination [...] It might be a false alarm, and there is no reason for them to worry about it, when I'm not even worried about it.

Woman, 74, single: It was such a positive experience. They told me during the whole procedure what they saw, and they blew up and removed some tiny little polyps.

Jane, 61, married: It is up to you to decide whether you want to be screened, but I think it is silly if you don't participate. We all pay for this in the end. In fact I think you have no right to say no.

Discussion

Desire to get screened – and cleared!
- Pressure on healthcare system to provide testing for people to confirm their (good) health?
- Perceived obligation: informed choice?

Conclusion

- Coping during waiting period includes symptom appraisal and communication strategies
- Patient involvement during colonoscopy may support trust in validity of result
- A "false alarm" for cancer may not decrease motivation for subsequent screening

The authors declare no conflicts of interest.

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Samlivsstatus, uddannelse og indkomst har betydning for kræftpatienters adgang til specialiseret palliativ indsats i Danmark

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BAGGRUND

I Danmark foregår specialiseret palliativ indsats (SPI) på hospitaler (palliative teams/enheder) og hospicer, og SPI er tidligere fundet værdifuld for patienter og deres pårørende.
I Danmark er viden om adgang til SPI begrænset, og internationale studier har fundet divergerende resultater i forhold til samlivsstatus, uddannelse og indkomst.

FORMÅL

Studiets formål var at undersøge, om adgang til specialiseret palliativ indsats (SPI) samlet og institutionsspecifikt (hospital og hospice) er associeret med samlivsstatus, uddannelse og indkomst.

METODE OG MATERIALE

Studiepopulationen var de personer, der døde af kræft i Danmark i 2010-12 (se figur 1). Registerstudiet var baseret på følgende registre, der alle har en høj datakomplethed og validitet undtagen Uddannelsesregistret, der har en lavere datakomplethed:

- *Dansk Palliativ Database (national klinisk kvalitetsdatabase)*
- *Dødsårsagsregisteret*
- *Det Centrale Personregister*
- *Cancerregisteret*
- *Uddannelsesregisteret*
- *Indkomstregisteret*

Logistisk regressionsanalyse blev anvendt til at undersøge sammenhængen mellem adgang og hhv. samlivsstatus, uddannelse og indkomst og både analyseret ujusteret og justeret (køn, alder, region, kræftdiagnose og samlivsstatus). Standardiserede absolutte prævalenser blev beregnet for samlivsstatus standardiseret i forhold til køn, alder, region og kræftdiagnose.

Figure 1. Flowchart over studiepopulationen

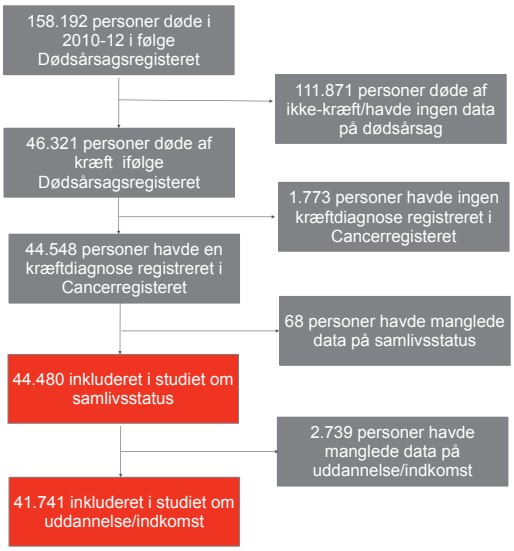
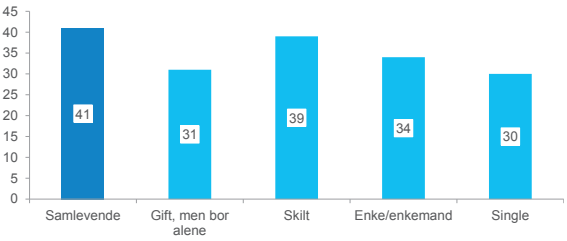


Figure 2. Standardiserede absolutte prævalenser for samlivsstatus (%)



RESULTATER

Adgang til SPI samlet var lavere for patienter, der boede alene sammenlignet med patienter, der var samboende (fx ugifte patienter 30% versus samboende patienter 41%, figur 2). Opdelt på institution var der højere adgang til palliative teams/enheder for patienter, der var samboende og lavere adgang til hospice.

Tabel 1. Adgang til specialiseret palliativ indsats samlet og institutionsopdelt, justeret for køn, alder, kræftdiagnose, region og samlivsstatus

	Adgang til specialiseret palliativ indsats Odds ratio (95%KI)		
	Samlet	**Hospital**	**Hospice**
Uddannelse:			
Grundskole	1 (reference)	1	1
Faglært	1,2 (1,1-1,2)	1,1 (1,0-1,2)	1,3 (1,2-1,4)
Kort teoretisk	1,3 (1,2-1,5)	1,2 (1,0-1,4)	1,6 (1,4-1,9)
Lang teoretisk	1,5 (1,4-1,6)	1,3 (1,2-1,4)	1,7 (1,6-1,8)
Akademiker	1,7 (1,5-1,9)	1,5 (1,3-1,7)	1,7 (1,5-2,0)
Indkomst:			
1.Kvartil	1	1	1
2.Kvartil	1,1 (1,0-1,2)	1,1 (1,0-1,1)	1,2 (1,0-1,2)
3.Kvartil	1,2 (1,1-1,3)	1,1 (1,0-1,1)	1,4 (1,3-1,5)
4.Kvartil	1,5 (1,4-1,6)	1,2 (1,1-1,3)	1,7 (1,5-1,8)

Sammenlignet med patienter med grundskolen havde akademikere større chance for at få adgang til SPI (Odds ratio =1,7). For indkomst havde patienter i den højeste indkomstkvartil større chance for at få adgang til SPI sammenlignet med patienter i den laveste indkomstkvartil (odds ratio = 1,5) – mest udtalt for hospice. I analysen, der medtog både indkomst og uddannelse, blev der for hvert uddannelsesniveau fundet stigende adgang til SPI med stigende indkomst, med undtagelse af akademikere hvor adgangen var høj i både laveste og højeste indkomstkvartil (odds ratio= 2,0).

KONKLUSION

Dette studie, baseret på unikke danske registre, viser, at adgang til SPI var lavere for patienter, der boede alene, 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 – hvor der er utilstrækkelig kapacitet, og det formentlig er de mest ressourcestærke patienter, der er bedst til at navigere i sundhedsvæsenet.

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Tumor-infiltrating lymphocytes predicts improved overall survival after post-mastectomy radiotherapy

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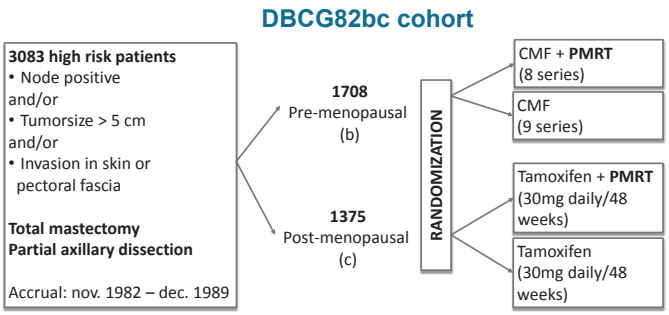
Background and aim

- Breast cancers (BC) are not very immunogenic
- 10% have "high levels" of tumor infiltrating lymphocytes (TILs)
- "High level" of TILs is:
  - associated with improved recurrence free- and overall survival (OS) in especially certain subtypes of BC
  - found to predict response to neo-adjuvant 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 treated with mastectomy followed by adjuvant systemic treatment and randomized to RT or not

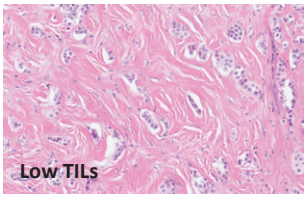
Materials and methods

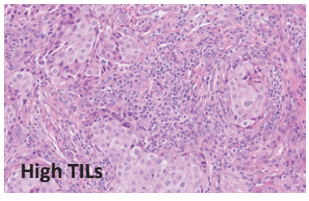
The material originated from a Danish Breast Cancer Group (DBCG) cohort based on a nationwide trial (**DBCG82bc**) conducted more than 25 years ago with the aim to investigate indications for post-mastectomy radiotherapy (PMRT)
The DBCG82bc cohort is associated with > 20 years of clinical follow-up



In 1011 pretreatment, tumor-containing paraffin-blocks:

- percentage of stromal TILs were estimated by 2 observers independently using HE staining's following international recommendations[1].
- ER, HER2, Ki67 was available from immunohistochemistry





TILs (%) = area of stromal tissue occupied by mononuclear inflammatory cells / total intra-tumoral stromal area

Statistics:
A competing risk model, Kaplan-Meier analysis and multivariate Cox regression analysis (MVA) were used for analyzing correlations between TILs and clinical outcome

Results

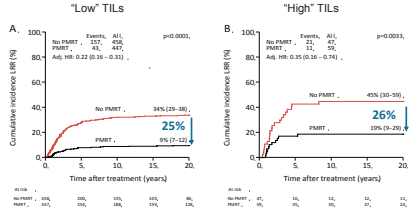
Evaluation of TILs:
Substantial interobserver agreement in predicting "high" *vs.* "low" TILs using a 30% cut off (Kappa value =0.69)

- 10.5% (106/1011) patients found to have "high" TILs

Predictive value of TILs in terms of benefit from PMRT:

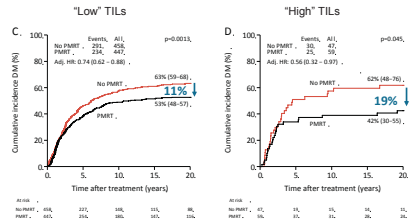
- A general benefit from PMRT could be found for all clinical endpoints regardless of level of TILs
- The benefit of PMRT to reduce the risk of loco-regional recurrence (LRR) was equal in the two TILs groups at 20 years (Fig A,B)

Loco-regional recurrences



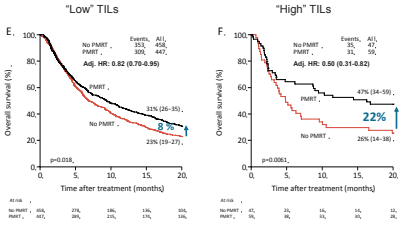
- A trend for greater reduction was observed for distant metastasis (DM) (11% *vs.* 19%, p=0.29) (Fig C,D)

Distant metastasis



- Significantly greater benefit from PMRT observed for "high" TILs patients as compared to "low" TILs patients with significantly improved OS at 20 years (test of interaction, p=0.024) (Fig E,F)

Overall survival



- The association for OS remained significant, when adjusting for clinical variables (ER, HER2, tumorsize, nodal status, age) in MVA (test of interaction: p=0.045)

Conclusions

Regarding benefit from RT, pre-treatment TILs in BC showed:
• no predictive information in terms of local control
• **"high levels" of TILs interacted with RT to further improve OS**

Findings may indicate that destruction and release of tumor antigens triggers a local immune response that induces a systemic effect outside the treatment field (**abscopal effect**)

1. Salgado et al., Ann Oncol 2015;26:259-271

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Novel DNA methylation markers show high sensitivity and specificity for blood-based detection of colorectal cancer

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Background and aim

Colorectal cancer (CRC) **screening** can **reduce mortality** and morbidity. Current screening tools are fecal occult blood testing (**FOBT**) and/or **endoscopy**. However, both tools suffer from **low compliance.** Therefore, development of **new screening tests** with high compliance and great performance is still warranted.

This study aimed to develop a **minimally-invasive** CRC screening test based on **blood** samples. As biomarkers, aberrant methylations associated to CRC in **cell-free DNA** (cfDNA), that circulate the blood, were chosen.

Methods

Figure 1: Flow chart of biomarker discovery and development

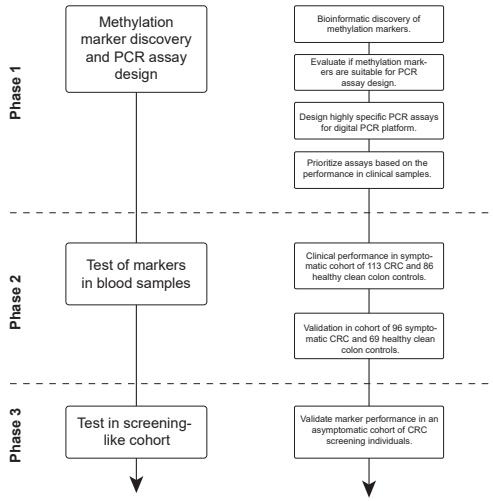

Figure 1: Flow chart of biomarker discovery and development. **Phase 1**) Discovery of aberrant methylation patterns associated to CRC and the design of PCR markers for these. After the bioinformatic discovery, the regions surrounding the candidate methylation sites were evaluated and PCR assays were designed to candidate regions. The sensitivity and specificity of the candidate PCR assays were reviewed using DNA from CRC tissue and leucocyte DNA from healthy blood donors. Assays with a sensitivity >90% and a specificity of 100% were prioritized. **Phase 2)** Methylation marker assays were tested on cfDNA from a symptomatic cohort of 113 CRC cases and 86 controls with clean colonoscopies. The performance was validated in 93 symptomatic CRC cases and 69 clean colon controls. **Phase 3)** Markers will be tested in an independent asymptomatic cohort comprising CRC cases, adenomas, and controls selected from a cohort of Danish CRC screening individuals.

Discovery: Analysis of methylation patterns from Illumina 450K arrays in >4000 samples. Selection of CRC associated aberrant methylations.

Marker design: Digital PCR assays were designed for selected DNA methylations and tested. The three best performing assays were chosen for analysis in clinical blood samples.

Test in clinical cohort: Analysis of marker performance in blood samples from 113 symptomatic CRC cases and 86 healthy clean colon controls.

Validation in clinical cohort: Validation of performance in independent cohort of 93 symptomatic CRC cases and 69 healthy clean colon controls.

Results

Figure 2: Analysis of marker performance in blood samples

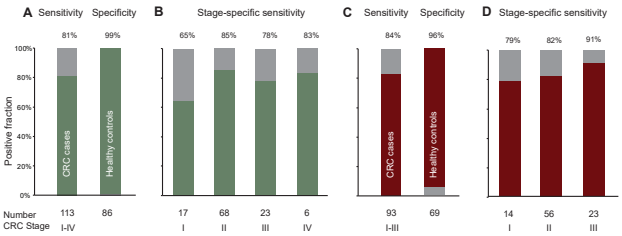

Figure 2: Overall sensitivity and specificity in clinical cohorts of cases and controls. As cases, symptomatic CRC cancers found after endoscopy were used. As controls, healthy individuals with clean colonoscopy were used. Individuals were selected from the Endoscopy II or Endoscopy III cohorts.Though cases and controls were age matched, cases had a higher median age than controls. cfDNA from two blood samples of 10 ml each were pooled and analysed with the methylation marker PCR assays on a digital PCR platform. Samples were called positive if two of the three markers were positive in the PCR reaction.
A) Proportion of positive CRC cases (stage I-IV) and controls in the first clinical test cohort. B) Sensitivity in CRC cases stratified by tumor stage in the test cohort. C) Proportion of positive CRC cases (stage I-III) and controls in the clinical validation cohort. D) Sensitivity in CRC cases stratified by tumor stage in the validation cohort.
In comparison, the FOBT test used in the Danish CRC screening program has a sensitivity ranging from 62-75 and a specificity >96%.

Optimization

Figure 3: Design strategy for marker optimization

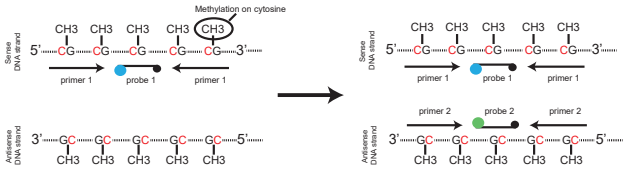

Figure 3: cfDNA consists of small double stranded DNA fragments. The two strands are complementary to one another (so-called 'sense' and 'antisense'). The three original PCR markers were designed to anneal to only one of the strands (the sense strand). As such, the antisense strand information of CRC specific methylation was un-exploited in the PCR reactions. To exploit the antisense strand as well, new PCR markers were designed to anneal to both to the sense strand and to the antisense strand. In theory, this would double the PCR signal intensity, because twice as many single cfDNA strands were now targeted. Further, it would help exploit all cfDNA in the sample. The latter is crucial in a CRC screening setting, where tumors release very little cfDNA to the blood because they are small and/or low stage cancers. This optimization could therefore enable markers to perform well in a screening setting, fulfilling the study aim. Optimized assays were made for two of te three markers.

Figure 4: Analysis of performance after optimization

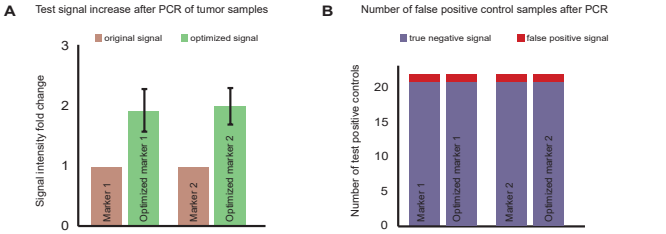

Figure 4: Optimized PCR markers were developed for two of three assays. Their performance was compared against the original markers on paired clinical samples.
A) Sensitivity was compared between the original markers and the optimized markers on tissue samples from 24 CRCs. The test signal intensity was calculated for all samples and the PCR signal from the original assays were set as reference. The signal intensity for the optimized assays was almost twice as high for the two markers. Whiskers indicate the standard deviation in the normally distributed data across all 24 samples. Samples were called positive if two of the three markers were positive in the PCR reaction.
B) Specificity was likewise compared between original and optimized markers in leucocyte DNA from 22 healthy controls. The number of false positive test results did not increase for the two markers.

Conclusion

cfDNA methylation markers can be used for CRC **detection** in blood with **high sensitivity** and **specificity** and results can be **validated**. **Optimization** is possible and initial studies indicate that this will **enable** even better performance. Validation of the improved markers in screening individuals are ongoing.

Conclusively, cfDNA-based methylation markers have the potential to **supplement** the current CRC screening program as blood-based alternatives to FOBT or as **triage** tool before endoscopy. Further, they show promise as stand-alone CRC screening tests.

Differential diagnostic impact of DNA methylation profiling on brain tumor classification

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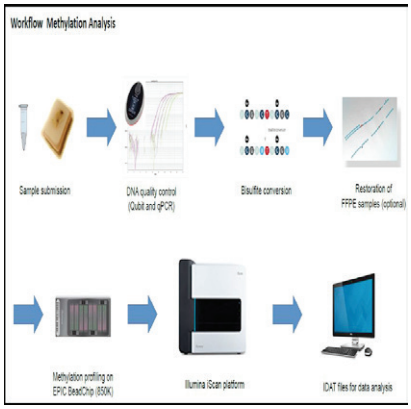
INTRODUCTION

Until very recently diagnostics of tumors of the central nervous system (CNS) has mainly been based on microscopy. However, some brain tumors are defined by imprecise diagnostic histological criteria leading to interobserver variation with detrimental consequences for the patients. New diagnostic tools are therefore required for more precise brain tumor diagnostics. DNA methylation profiling is a new promising approach for improved brain tumor classification.

We have in a prospective study investigated the differential diagnostic impact of a DNA methylation-based classifier tool in a clinico-pathological setting.

MATERIALS AND METHODS

Fig. 1 DNA (FFPE/fresh tissue samples) is processed in a four-day workflow including multiple steps (quantitation and quality control, bisulfite conversion, amplification, fragmentation, hybridization, chip preparation and scanning).

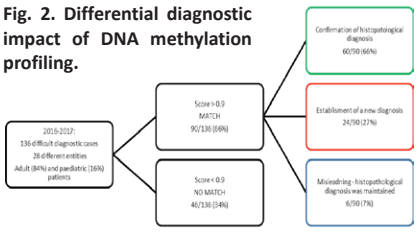


We prospectively collected tissue from 136 brain tumor cases, where the initial diagnostic workup had led to unclarified diagnoses.

DNA methylation profiling was performed using the EPIC BeadChip (850K). Methylation profiles 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.

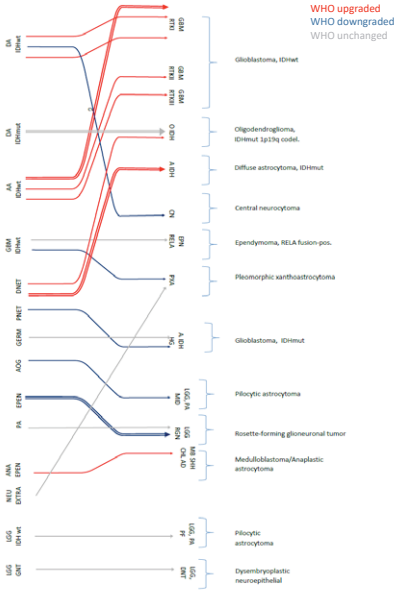
RESULTS

Fig. 2. Differential diagnostic impact of DNA methylation profiling.



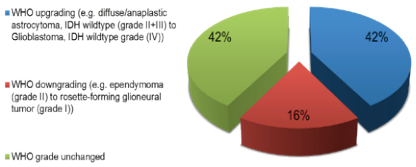
- For 90 of the 136 brain tumors (66%) a significant match to a methylation class was reached (score > 0.9) – the remaining 46 brain tumors (34%) could not be matched to a methylation class.
- For 60 of the 90 brain tumors (66%) the result of the methylation profiling corresponded very well to the histopathologic diagnosis.
- For 24 of the 90 brain tumors (27%) there were discrepancy between the histopathologic diagnosis and methylation class and a new better diagnosis were established in favor of the methylation profiling result. Besides significant methylation profiling scores (>0.9) the change in diagnosis were based on immunohistochemical findings and next-generation sequencing results.
- For 6 of the 90 brain tumors (7%) the methylation profiling was interpreted as misleading and the initial diagnosis was maintained.

Fig. 3 Establishment of new and better diagnosis – Histopathologic diagnosis (left) and methylation class and a new better diagnosis (right).



RESULTS (continued)

Fig. 4 Clinical impact of DNA methylation profiling



A change in WHO tumor grade, among the 24 brain tumors with a changed diagnosis, was observed in 58 % of the tumors, with downgrading of 16 % and upgrading of 42%.

CONCLUSION

- **DNA methylation profiling is a powerful diagnostic tool for brain tumor classification - especially in challenging diagnostic cases, where morphological and genetic features are inconclusive.**
- **DNA methylation profiling improves integrated brain tumor diagnostics by providing molecular information.**
- **DNA methylation profiling provides more precise brain diagnoses with allocation of patients to the correct treatment.**
- **DNA methylation profiling reduces over- and undertreatment.**

ACKNOWLEDGEMENTS

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- Main supervisor, Prof. Bjarne Winther Kristensen
- Henning B. Boldt, PhD, Molecular Biologist
- René Sørensen & Tobias Teken Christensen, Biomedical Laboratory Scientists

Collaborators:
- Denmark (Rigshospitalet, Aalborg University Hospital, Aarhus University Hospital)
- Sweden (Karolinska University Hospital)
- Finland (Turku University Hospital)

Methylation profiling
UniversitätsKlinikum Heidelberg
- A. von Deimling
- D. Capper

SODIUM FLUORESCEIN GUIDED SURGERY EXTENDS GLIOMA RESECTION GRADES

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INTRODUCTION

Glioblastoma continues to have a poor prognosis with a median survival of 12-15 months. Current treatment is largest possible extent of resection of tumor followed by concomitant chemo- and radiotherapy.

Sodium fluorescein (SF) is a non-toxic dye. In the brain it passes through a deficient blood-brain barrier and is comparable to contrast-enhanced tissue on MRi.

Aim: Can SF assist the surgeon and increase the extent of resection compared to current treatment.

METHODS

Descriptive study including patients suspected of glioblastoma.

Patients would receive 200mg SF intravenously after induction of anaesthesia and surgery was performed alternating between YELLOW 560 filter and white light.

Three neurosurgeons graded SFs ability to locate and remove tumor tissue from one to four.

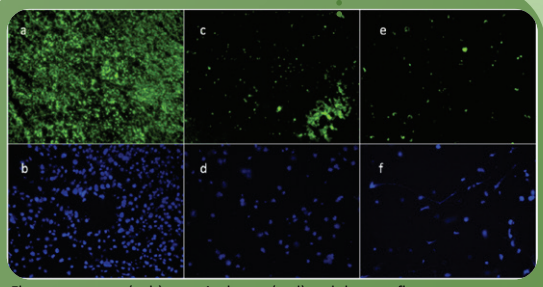
Neuroradiologist compared pre- and post-OP MRi and graded extend of resection according to RANO criterias.

Biopsies were taken in fluorescent, non-fluorescent and marginal zone tissue to investigate fluorescein distribution in the tissue

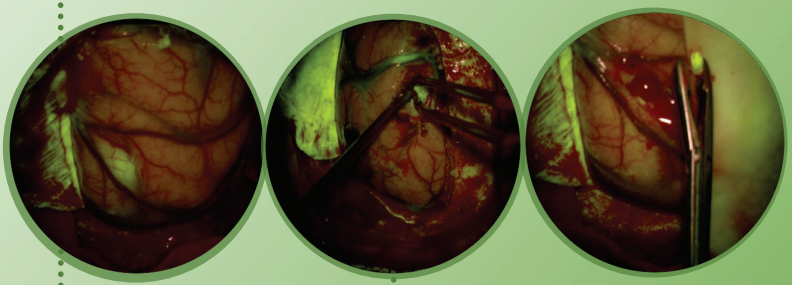
RESULTS

13 patients were included. No adverse effects were registered.

- Total resection rate was 77% (95% CI: 46-95%). In comparison, nationwide resection rate was 38% (33-44).
- Surgeons evaluation of SF usability for tumor localization was a median 3.8 out of 4. Surgeons also found SF useful in tumor removal (median 3.7).
- Biopsies taken showed an observable correlation between the grade of fluorescence and cellularity of malignant tumor cells.



Fluorescent area (a+b), marginal zone (c+d) and the non-fluorescent area (e+f) showing the correlation between SF (green) and tumor cells (blue).



CONCLUSION

Although performed in a selected patient group, our study indicates using sodium fluorescein during glioblastoma surgery increases the extent of resection.
The surgeons found sodium fluorescein highly usable.
Currently, randomized trials with international collaborators are planned to verify the results.

SDU

OUH Odense Universitetshospital

Poster #96

Hybrid imaging with PET/MR in oncology

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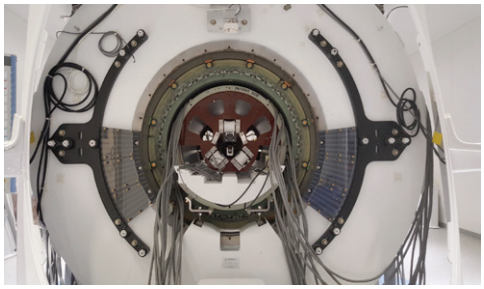
Introduction

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 in a single session. With the introduction of MRI instead of the more common PET/CT gives new possibilities due to the superior soft-tissue contrast of MRI compared to CT. MRI is also not only an anatomical imaging modality but also provides functional imaging which add additional diagnostic information to value of oncological patients in need of specialized treatment plans or monitoring of treatment response.

PET/MR scanner installation

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



Simultaneous PET/MR for glioma

The use of a PET/MR enables simultaneous MR and PET imaging in a single session allowing for direct comparison of both anatomical and functional MR with dynamic PET. An example of imaging in subject suspected of glioma using fluoro-ethyl-tyrosine (FET) PET and both anatomical MR (T2W) and functional imaging (DWI) is shown below in Figure 3.

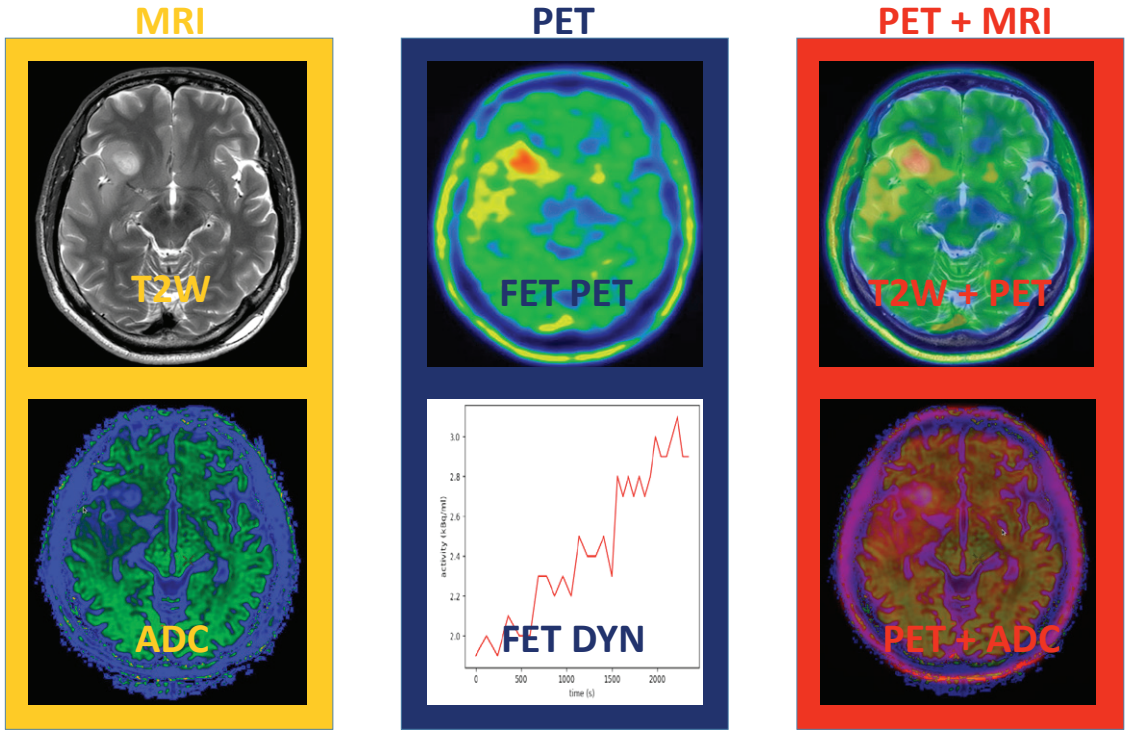


Figure 3. T2W MRI and Fluoro-ethyl-tyrosine (FET) PET in a true simultaneous acquisition allows for exact registration between MR and PET in a single session.

Future work

Future work will include PET/MR imaging in neurology, head and neck and prostate cancer along with correlation of MRI functional parameters with PET dynamic parameters.

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Region of Southern Denmark

Nuclear Medicine

Predictive biomarkers for malignant pleural mesothelioma

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Introduction

Malignant Pleural Mesothelioma (MPM) is an asbestos-related, aggressive malignancy with a median survival of 12 months[1]. 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[2,3]. 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.

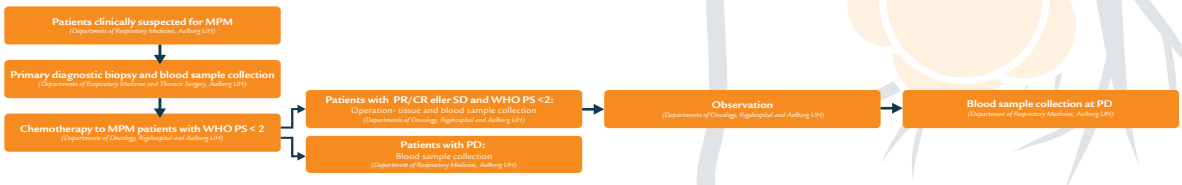
Results

Currently, 28 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 with a predictive and prognostic value in tumor and in serum for chemotherapy will hopefully contribute to more personalized and more effective MPM treatment and thus, reduce excessive treatment and unnecessary costs.

Figure 1. Graphic presentation of Materials and Methods



WHO PS=World Health Organization Performance Status
PR=Partial Response
CR=Complete Response
SD=Stable Disease
PD=Progression of Disease
Aalborg UH=Aalborg University Hospital

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Core needle biopsies of renal masses; prevention of overtreatment with low complications rate

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•Background

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

•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. In total, five of the 240 procedures (2.1%) resulted in 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.

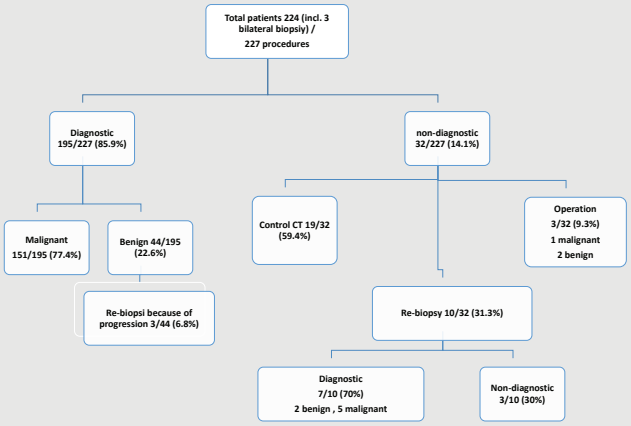
Baseline characteristics

	Study population n = 129	Malign biopsies n = 77	Benign biopsies n = 35	Inconclusive biopsies† n = 17	*p* value*
Age at diagnosis, years, median (IQR)	68.8 (59.8-73.4)	67.4 (58.3-72.9)	68.8 (60.3-77.0)	70.7 (66.5-73.6)	0.52
Tumour size at CT scan, mm, median (IQR)	28 (18-36)	30 (20-36)	25 (17-35)	20 (17-30)	0.08
Number of biopsies, median (IQR)	3 (2-3)	3 (2-3)	3 (2-3)	3 (2-3)	0.66
Gender, n (%)					0.07
Male	82 (63.6)	54 (70.1)	21 (60.0)	7 (41.2)	
Female	47 (36.4)	23 (29.9)	14 (40.0)	10 (58.8)	
Side, n (%)					0.24
Right kidney	65 (50.4)	38 (49.4)	21 (60.0)	6 (35.3)	
Left kidney	64 (49.6)	39 (50.6)	14 (40.0)	11 (64.7)	

Abbreviations: CT = computed tomography; IQR = inter quartile range.
† Inconclusive biopsies= Material not representative and Normal kidney tissue
*The *p* value represents the chi-square test for categorical variables and the Kruskal-Wallis Test for continuous variables.

•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.



Distribution of tumor stage and treatment strategy (224 patients)

Stage	Tumor size (cm)			
	<4 cm	4-7 cm	>7 cm	All, N (%)
Localized tumor	103	35	9	147 (65.6%)
Metastatic disease	20	30	27	77 (34.4%)
Treatment				
Active surveillance	40	7	1	48 (21.5%)
Partial nephrectomy	43	17	0	60 (26.8%)
Radiofrequency ablation	4	0	0	4 (1.8 %)
Nephrectomy	9	16	10	35 (15.6%)
Oncological treatment	12	18	19	49 (21.8%)
No treatment	15	8	5	28 (12.5%)

•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.

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TOX expression in patients with Mycosis fungoides – a potential diagnostic marker?

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Introduction

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). MF is both a clinical and histological challenge because of the morphological and histological similarities to benign inflammatory dermatitis (BID).TOX plays an important role in regulating T-cell development and has been implicated as an oncogenic marker in CTCL, being significantly increased in MF compared to reactive skin conditions, indicating a potential role of TOX as a useful diagnostic marker.

Aim

To investigate TOX expression in patients with 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 Pathology, Region Zealand in the years 1990 to 2016. Skin biopsies with dermatitis and normal skin were used as controls. TOX mRNA was analyzed with a customized NanoString gene expression panel and TOX protein expression was detected with immuno-histochemical staining and scanned (Leica 400SCN) and digitally image analyzed with a TissueIA (Leica Microsystems) algorithm adjusted to the specific immuno-histochemical staining. * indicates $p < 0.05$.

Contact

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Results

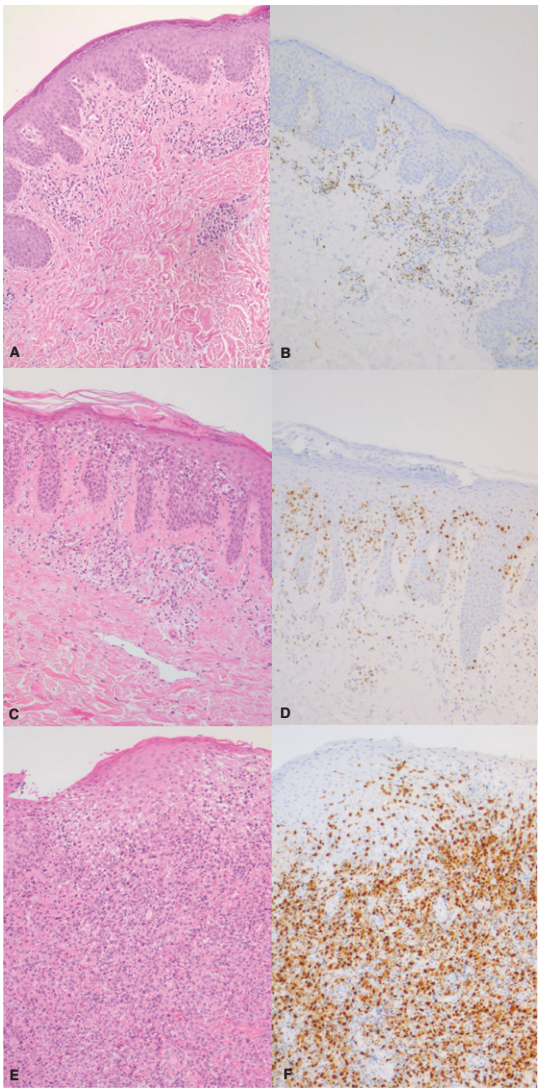

Fig. 1. Characteristic histopathological features of dermatitis (**A+B**), patch of Mycosis fungoides (**C+D**) and tumor of Mycosis fungoides (**E+F**). (**A, C, E,** Hematoxylin-eosin stain); (**B, D, F**, Immunohistochemical TOX stain); (All magnifications X10)

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Danske Kræftforskningsdage

Conclusion

Our study reveals that TOX is overexpressed in early MF compared to BID. Furthermore, the mRNA and protein expression increases with advanced disease stage. These findings indicate that TOX expression can be of diagnostic value in early stage disease.

Fig 1. TOX mRNA expression

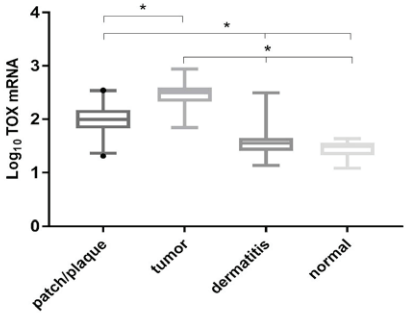


Fig 2. IHC – TOX positive cells

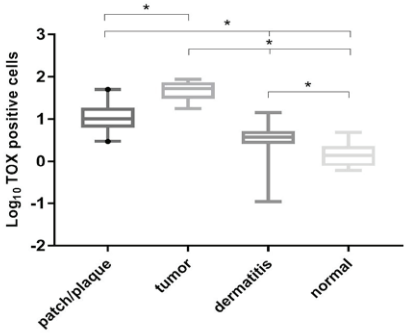
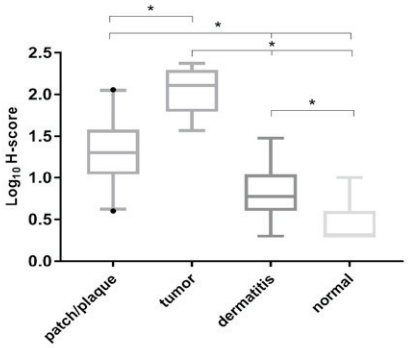


Fig 3. IHC – TOX H-score



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Stråleføls omhed hos patienter med hoved-halskræft

Jacob Lilja-Fischer[1,2], Benedicte Ulhøi[3], Magnus Stougaard[3], Pernille Lassen[4], Mette Thomsen[5], Viveque Nielsen[6], Torben Steiniche[3], Jan Alsner[1], Jens Overgaard[1].

[1]Afdeling for eksperimentel klinisk onkologi, [2]Øre-, næse- og halskirurgi, [3]Patologi, [4]Kræftafdelingen, [5]Medicinsk fysik; Aarhus Universitetshospital. [6]Øre-Næse-Halsafdelingen, Odense Universitetshospital.

Baggrund

- Der er i Danmark ca. 450 tilfælde årligt af kræft i mundsvælget. Antallet er steget kraftigt de seneste årtier.
- Langt de fleste tilfælde skyldes *Humant papillomavirus* (HPV), de resterende tilfælde primært tobaksrygning.
- Standardbehandlingen er strålebehandling. Ved HPV-positiv sygdom er kræftsvulsten ofte særdeles *strålefølsom*, og prognosen er da favorabel. Dette er dog ikke tilfældet hos alle.
- For at øge overlevelsen og mindske bivirkningerne er der behov for at give patienterne en mere individuel behandling, men der mangler viden om sygdommens særlige biologi.

Formål

- Projektets formål er at overføre kræftsvulster fra patienter med mundsvælgkræft til mus, for på den måde at skabe livagtige modeller til brug for eksperimentel kræftforskning.
- Kræftsvulsterne undersøges mikroskopisk og genetisk, og stråleføls omheden undersøges eksperimentelt.

Metode

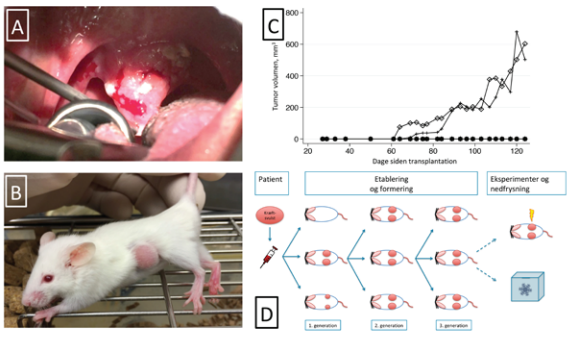
- Frisk tumorvæv implanteres under huden i immunsvækkede mus, og overføres til nye generationer af mus (**Figur 1**).
- Kræftsvulsterne og patientens originale svulst undersøges mikroskopisk samt med immunhistokemi og DNA sekventering.
- Kræftsvulsternes stråleføls omhed bestemmes eksperimentelt ved bestråling ved forskellige doser (0, 4, 6 og 8 *Gray*).

Konklusion

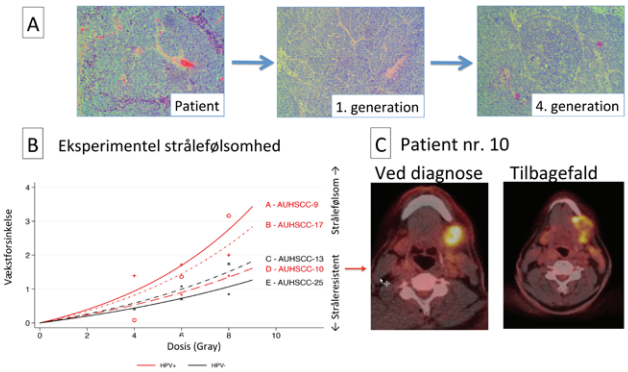
- Kræft i mundsvælget forårsaget af HPV er i kraftig stigning.
- Denne kræftform kan undersøges eksperimentelt ved at overføre kræftvæv fra patienter til mus, hvor de fleste kræftsvulster beholder deres mikroskopiske og genetiske kendetegn.
- Den eksperimentelle stråleføls omhed stemmer overens med den forventede og klinisk observerede stråleføls omhed.
- Denne eksperimentelle model kan anvendes til videre forskning i kræftsygdommens biologi og behandling.

Resultater

- Af kræftvæv fra 34 patienter etablerede vi 12 eksperimentelle kræftmodeller, hvor mikroskopiske og immunhistokemiske kendetegn var velbevaret.
- Ved DNA sekventering var der god overenstemmelse mellem patienternes originale kræftsvulster og de eksperimentelle kræftsvulster, med vigtige *driver-mutationer* bevaret.
- Som forventet var HPV-positive kræftsvulster mere stråleføls omme end HPV-negative.
- Én HPV-positiv kræftsvulst var dog mere stråleresistent, og denne patient har desværre også haft tilbagefald af sin sygdom (**Figur 2**).



Figur 1. A. Kræftsvulst i mundsvælget. **B**. Kræftsvulsten etableret i en immunsvækket mus. **C**. Vækstmønster af kræftsvulsten overført til flere mus. **D**. Overblik over etablering, formering og eksperimenter med kræftsvulster overført til mus.



Figur 2. A. Kræftsvulsten bevarer sine mikroskopiske kendetegn. **B**. Stråleføls omhed af patienternes kræftsvulster bestemt ved bestråling af kræftvævet i mus. **C**. Patient nr. 10 var HPV-positiv men havde eksperimentelt en relativt stråleresistent kræftsvulst, og fik senere et tilbagefald af kræftsygdommen.

CENTER FOR CANCER IMMUNE THERAPY

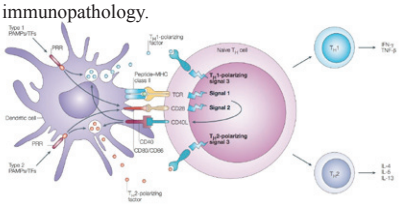
Secreted IL-12p70 from long-term activated dendritic cells is lost concomitant with their apoptosis and release of IL-10

Laura Stentoft Carstensen, Andreas Obers, Inge Marie Svane, Morten Hansen

Center for Cancer Immune Therapy, Department of Haematology and Department of Oncology, Copenhagen University Hospital, Herlev

Background

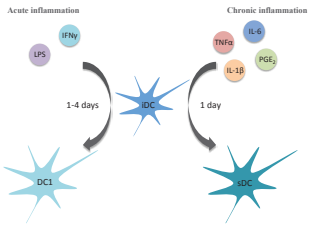
The balance between peripheral tolerance and adaptive immunity has profound implications in several disease settings. Interleukin (IL)-12 plays a major role in immunity to intracellular pathogens and cancer by controlling IFNγ-dependent adaptive immunity. Upon selected stimuli, dendritic cells (DCs) transiently secrete the bioactive IL-12p70 heterodimer which is tightly balanced with secreted IL-10, to avoid immunopathology.



DC-mediated activation of a naïve CD4⁺ T cell

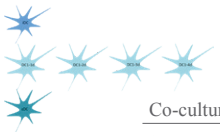
Materials and methods

Maturation of monocyte-derived DCs

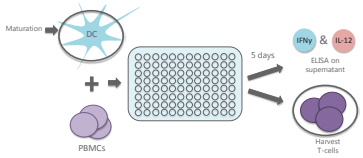


Long-term exposure to bacterial lipopolysaccharide (LPS) and interferon (IFN)γ was evaluated on human monocyte-derived dendritic cells (DCs).

Six different DC subtypes

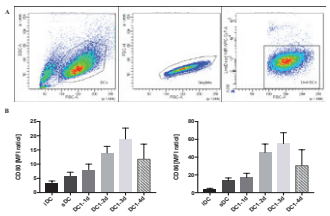


Co-culture with allogeneic T cells

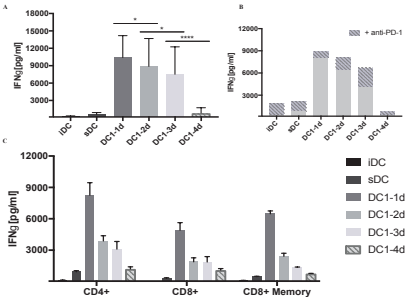


The activated DCs were co-cultured with allogeneic T cells present in peripheral blood mononuclear cells (PBMCs) from healthy volunteers.

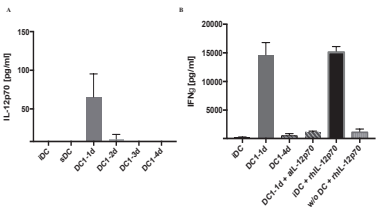
Results



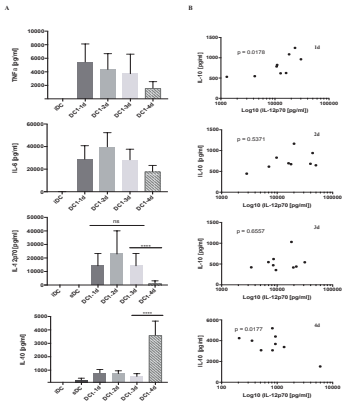
Expression of CD80, CD86 during extended DC maturation (n = 6 donors).



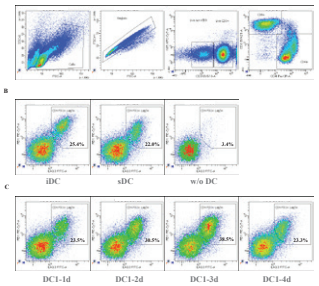
IFNγ release from co-cultures with long-term activated DCs is reduced (n = 9 donor pairs). Pembrolizumab, an anti-PD-1 antibody, enhanced the IFNγ responses in all co-cultures.



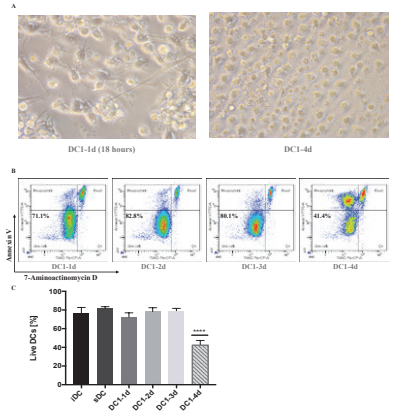
IL-12p70 secreted by DCs in co-culture mediates IFNγ response (n = 3 donor pairs).



Cytokine concentrations in DC supernatants during extended maturation (n = 7 donors).



Flow cytometric analysis of expanded lymphocytes after co-culture with DCs (n = 2 donor pairs).



Apoptosis is induced in DCs after four days of stimulation with LPS and IFNγ (n = 4 donor pairs).

Conclusions and perspectives

- Extended exposure to LPS and IFNγ affected the phenotype, cytokine production, cell activating capacity and viability of human monocyte-derived DCs.
- It is under current investigation whether IL-12p70 degrades intrinsically after four days in culture medium or if apoptotic DCs actively stimulate the degradation of IL-12p70

Further information

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"Fra kold til varm"

Kan varmebehandling øge kræftknuders følsomhed overfor immunterapi?

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Afd. for Eksperimentel Klinisk Onkologi
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Introduktion

- Nogle kræfttyper er mere **immunogene** (varme) end andre.
- De **responderer på immunterapi.**
- Er det muligt at inducere en immunologisk reaktion i de **mindre/ikke immunogene** (kolde) **kræfttyper**?
- Kan dette gøres med **lokal varmebehandling?**
- Hvad er **mekanismen**?

Baggrund

- **Varmebehandling/hypertermi** er **temp. 40-45 °C**
  - **Direkte** celledød
    - Celler i **iltfattigt** og **surt** tumormiljø
  - **Indirekte** celledød
    - Nedsætter **blodgennemstrømning**
    - Inducerer **immunologisk reaktion**

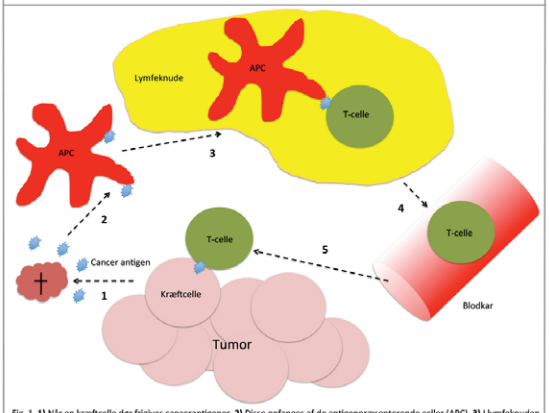

Fig. 1. **1)** Når en kræftcelle dør frigives cancerantigener. **2)** Disse opfanges af de antigenpræsenterende celler (APC). **3)** I lymfeknuden præsenterer APC cancerantigenet til T-cellen, denne aktiveres og **4)** følger blodet ud til tumoren (kræftknuden), **5)** hvor den genkender cancerantigenet, binder sig til kræftcellen, og dræber denne.

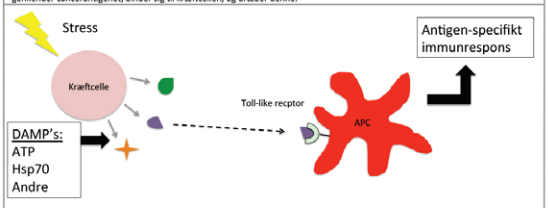

Fig. 2. Stress i form af feks. varme- eller strålebehandling kan medføre frigivelse af DAMP's (Damage Associated Molecular Patterns) fra den døende kræftcelle. Disse kan bindes til Toll-like receptorer på APC (AntigenPræsenterende Celle) og føre til et antigenspecifikt immunrespons.

Metode

- CDF1 mus blev podet med **C3H-mammacarcinom (brystkræft)** på højre bagpote
- Ved tumorstørrelse på 200mm^3 blev musen inkluderet i forsøg med enten **immunterapi** (checkpoint inhibitor Anti-CTLA-4-antistof (Ab)) i varierende frekvenser +/- **lokal varmebehandling** (42,5°C i 1 time):

Grupper	Dag 0	Dag 1	Dag 2	Dag 3	Dag 4
Kontrol		PBS	PBS	PBS	PBS
Antistof dag 1		Ab	PBS	PBS	PBS
Antistof dag 1, 3		Ab	PBS	Ab	PBS
Antistof dag 1-4		Ab	Ab	Ab	Ab
Varme alene	Varme	PBS	PBS	PBS	PBS
Varme + Antistof dag 1	Varme	Ab	PBS	PBS	PBS
Varme + Antistof dag 1, 3	Varme	Ab	PBS	Ab	PBS
Varme + Antistof dag 1-4	Varme	Ab	Ab	Ab	Ab
Volumen		**0.02mL/g**	**0.02mL/g**	**0.02mL/g**	**0.02mL/g**

- Tumorstørrelse blev målt dagligt
- Endepunkt: Tumorvæksttid x 5 (TGT5)


Lokal varmebehandling i vandbad


Måling af tumorstørrelse

Resultater

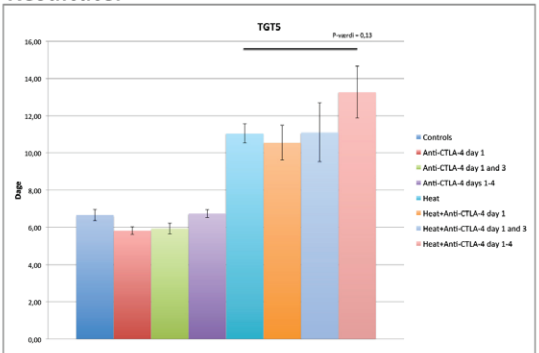

Fig. 3. Histogram visende tumorvæksttid x 5 (TGT5). Der sås ingen signifikant forskel for grupperne behandlet med Anti-CTLA-4-ab alene sammenlignet med de kontrolbehandlede. Varmebehandling alene forsinkede væksten. Varme kombineret med Anti-CTLA-4-ab dag 1-4 viste en tendens til længere vækststid, denne var dog ikke signifikant (p = 0,13).

Konklusion

- C3H-mammacancer **responderer ikke** på behandling med anti-CTLA-4-ab, den er kold. Kombineret med **lokal varmebehandling** er der **måske en effekt** vurderet ud fra tumorvæksttid; den bliver varm. Yderligere eksperimenter for at belyse dette nærmere er planlagt.
- I igangværende eksperimenter undersøger vi **mekanismen** bag v.hj.a. immunhistokemiske analyser, der kan **identificere** og **kvantificere tumorinfiltrerende immunceller**.

Tak til

Teknisk personale
Inger Marie Horsman
Dorthe Grand
Maria L. Bech
Marianne Kristiansen

Kræftens Bekæmpelse

Aarhus University Hospital

CANCER IMPACT IN DENMARK
A nationwide register-based cohort study (CEDAR)

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[1]OPEN – Odense Patient data Explorative Network, Odense University Hospital and University of Southern Denmark, Odense, [2]ApHER – Institute of Applied Economics and Health Research, Copenhagen, [3]AstraZeneca, Copenhagen

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.

The CEDAR Study (Cancer Impact in Denmark) was initiated in December 2017 with the overall aim to characterize cancer subpopulations and the impact of cancer. The governance structure of CEDAR involves a Scientific Committee and supporting tumor-specific clinical and pathology specialists (Figure 1). Using the Danish Cancer Registry as the central 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 (Figure 2).

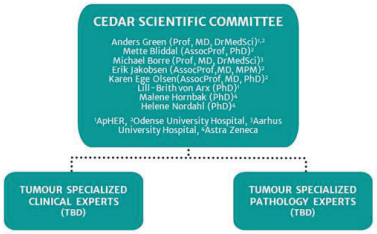


Figure 1 CEDAR study: Governance structure

Methods

The CEDAR study is a nationwide, observational 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. Patients are followed from date of first diagnosis until death or end of 2016. Analyses include aspects related to epidemiology, morphology, treatment patterns and associated clinical outcomes, together with cost-of-illness estimates and analyses of health care utilization.

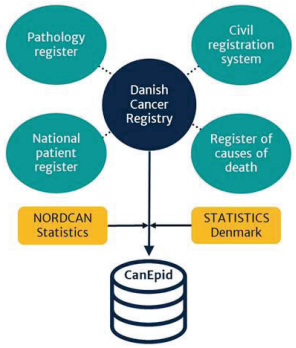


Figure 2 The CanEpid Research Database: Register sources and supplementary data. Linkage between registers is ensured by the unique personal identification number (CPR)

Results

Preliminary results arising from the CEDAR study include epidemiological profiles with forecasting models for cancer incidence, mortality, and prevalence to year 2030 (Figure 3). The five cancer forms concerned differ in terms of epidemiological profiles and trends over time and prevalence will generally increase substantially in the future.

Figure 3 Preliminary epidemiological results of the CEDAR study: Numbers of annual incidence, mortality and prevalence in the cancer forms included in the CEDAR study. Observed during 2005-2015 and predicted during 2016-2030

Conclusions

The CEDAR study represents an internationally unique resource for describing the impact of cancer for patients and society in a longitudinal real life setting. The resource may be further enriched by linkage with data in the 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 for comparative studies in the Nordic countries using standardized protocols and methods of analysis.

Presented at the Danish Cancer Research Days, 30. – 31. August 2018 , Odense, Denmark

Is Acute Pancreatitis a Risk Factor for Pancreatic Cancer?

A population-based matched cohort study

Jakob Kirkegård[1], Deirdre Cronin-Fenton[2], Uffe Heide-Jørgensen[2], Frank Viborg Mortensen[1]

[1] Department of Surgery, Section for Upper Gastrointestinal and HPB Surgery
[2] Department of Clinical Epidemiology

Aarhus University Hospital

1 BACKGROUND & AIM

- Pancreatic cancer is aggressive
- 50% dies within 6 months
- Early diagnosis is essential
- Few risk factors are identifed

We investigated if acute pancreatitis increases pancreatic cancer risk

4 POPULATION

Cases **41,669** | Controls **208,340**

55.8 years

54.7% ♂

5 CANCER RISK

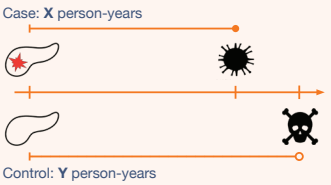
According to follow-up time

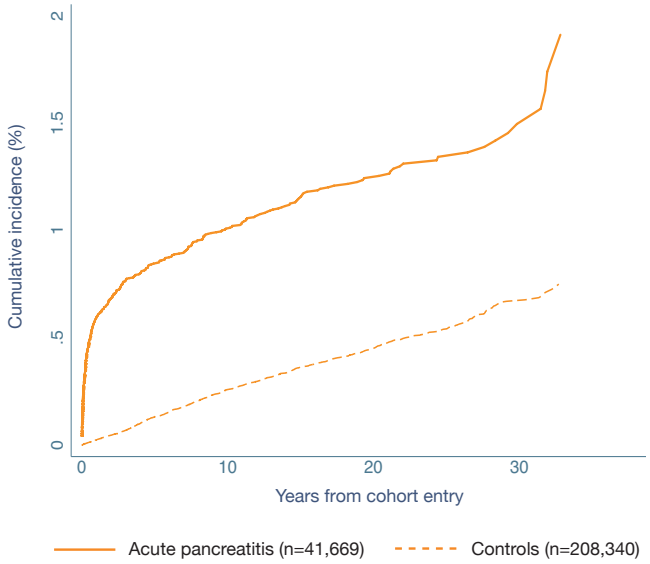
2-5 years: 2.4x

>5 years: 2.0x

2 METHODS

- Matched cohort study
- Population-based
- **Time-period**: 1980-2012
- **Exposure**: Acute pancreatitis
- **Controls**: Age- and sex-matched from the general population (1:5)
- **Survival analyses**: Cox regression





3 DATA SOURCES

- Danish National Patient Registry
- Danish Cancer Registry
- Danish Civil Registration System

6 CONCLUSION

Acute pancreatitis patients have a 2x higher risk of pancreatic cancer than the general population

Hydrochloro-thiazide, and risk of skin cancer

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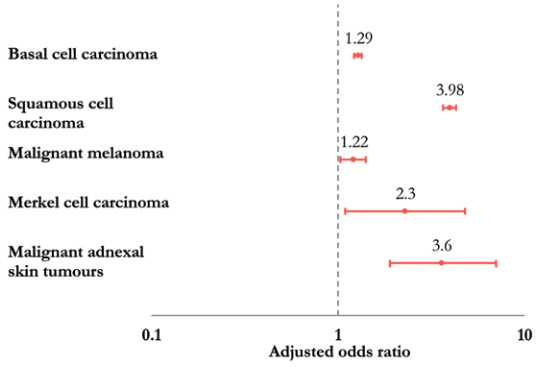
Background
Hydrochlorothiazide is one of the most frequently used diuretic and antihypertensive drugs in the United States and Western Europe. It has photosensitizing properties, and the International Agency of Research on Cancer, has categorized it as "possibly carcinogenic to humans".

Materials and Methods
In five separate case-control studies, we studied the association between use of hydrochlorothiazide and risk of basal cell carcinoma, squamous cell carcinoma, 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 hydrochlorothiazide use. We also examined dose-response effects and associations with the use of drugs with similar indications as hydrochlorothiazide.

Results
We observed a steep dose-response pattern for squamous cell carcinoma, with ORs reaching 7.38 (6.32-8.60) with use of ≥ 200,000 mg hydrochlorothiazide. 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 ≥200,000 mg hydrochlorothiazide. For melanoma, we found a weak association 1.22 (1.09-1.36) with hydrochlorothiazide use (≥50,000mg), driven by increased ORs for nodular 2.05 (1.54-2.72) and lentigo melanoma 1.61 (1.03-2.50).

The adjusted ORs for Merkel cell carcinoma and MAST associated with highest use (≥100,000mg) of hydrochlorothiazide 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 anti-hypertensives, including bendroflumethiazide (a thiazide with photosensitizing properties) yielded neutral associations for all outcomes.

Association between use of hydrochlorothiazide (>50,000 mg), and risk of skin cancer.



Conclusion
In conclusion, our results indicate that use of hydrochlorothiazide is associated with increased risk of all types of UV-dependent skin cancer and seems strongest for squamous cell carcinoma.

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#114


SDU NEWS
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USE OF ANTIPSYCHOTICS AND RISK OF BREAST CANCER
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Some antipsychotics increases prolactin levels, which might increase the risk of breast cancer. In a Danish case-control study based on 60,360 female breast cancer patients, long-term use (≥ 10,000 mg olanzapine equivalents) was associated with breast cancer, with an adjusted OR of 1.18 (95% CI, 1.06, 132) and a weak dose-response pattern. Associations were similar for first- and second-generation antipsychotics (ORs 1.17 and 1.11), but also for non-prolactin inducing antipsychotics (OR 1.17). Upon stratification, positive associations were seen for estrogen receptor positive but not for estrogen receptor negative cancers (OR 1.29 vs 0.92). Overall, our results do not suggest a clinically important association between antipsychotic use and risk of breast cancer.
www.antonpottegaard.dk/antipsychbreast.pdf
British Journal of Clinical Pharmacology
ORIGINAL ARTICLE
Use of antipsychotics and risk of breast cancer: a Danish nationwide case–control study
illustrated by Marie S.

DBCG DANISH BREAST CANCER GROUP

Risk factors of sentinel and non-sentinel lymph node metastases in patients with ductal carcinoma *in situ* of the breast

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Objective

Ductal carcinoma *in situ* (DCIS) of the breast is a non-invasive breast lesion that does not spread to the lymphatic system. However, unexplained axillary metastases have been detected in some patients with DCIS, possibly because of occult invasion or iatrogenic displacement of tumour cells.
The significance of these metastases is unknown.

Aim

To identify risk factors of sentinel lymph node (SN) and non-SN metastases, including the risk of iatrogenic displacement of tumour cells, in patients with DCIS. This to identify subgroups of patients where axillary surgery can safely be omitted.

Methods

Study design: Population-based register study.

Study period: 2001-2015.

Patients: Women with histologically pure DCIS lesions with (N=71) or without (N=1716) positive SN (SN with Isolated tumour cells, micro- or macrometastases). Data were retrieved from the Danish Breast Cancer Group.

Study variables: Age at diagnosis, year of diagnosis, size of DCIS lesion, Van Nuys classification, palpability and biopsy method (needle biopsy vs. excisional biopsy).

Statistics: Univariate and multivariable analyses, SAS statistical software version 7.11.

Results

Out of 1787 patients, 71 (4.0%) had positive SN.
Of these 71 patients,

- 15 (0.8%) showed macrometastases,
- 42 (2.4%) showed micrometastases and
- 14 (0.8%) showed isolated tumour cells.

Moreover, five patients with positive SN had a positive non-SN by axillary lymph node dissection.

Results of adjusted analysis showed that patients with positive SN

- were younger,
- had large sized DCIS lesions,
- had palpable DCIS lesions and
- had previously undergone excisional biopsy.

Patient and tumor characteristics and their associations with positive SN among 1787 Danish patients with DCIS who underwent SN biopsy during 2001-2015.

Variables	Negative SN n=1716 (%)	Positive SN n=71 (%)	Adjusted analysis* OR (95 % CI)	P value
Age (years)				
≤49	258 (92.1)	22 (7.9)	1.79 (1.04-3.10)	0.036
≥50	1458 (96.8)	49 (3.3)	1.00	
DCIS size (mm)				
<49	1450 (96.8)	48 (3.2)	1.00	0.002
≥50	266 (92.0)	23 (8.0)	2.34 (1.38-3.97)	
Palpability				
Yes	1289 (97.1)	38 (2.9)	1.00	0.0004
No	427 (92.8)	33 (7.17)	0.40 (0.24-0.67)	
Biopsy method				
Needle biopsy only	1550 (96.9)	50 (3.1)	1.00	<0.0001
Excisional biopsy	166 (88.8)	21 (11.2)	4.29 (2.47-7.43)	

Conclusion

The overall risk of positive SN in DCIS patients is low and less than 10% of these patients have a positive non-SN. This argues against the use of extensive axillary surgery in this group.

The odds of positive SN after an excisional biopsy is more than four-fold increased, indicating iatrogenic displacement of tumour cells. These patients should not be upstaged and should not be classified as having invasive carcinomas.

REGION The Capital Region of Denmark

#120

Department of Clinical Epidemiology

Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin-Receptor Blockers and the Risk of Acute Kidney Injury after Colorectal Cancer Surgery
A Population-Based Cohort Study

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Background

Angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin-receptor blockers (ARBs) are commonly used antihypertensive drugs with potential nephrotoxicity.

Acute kidney injury (AKI), defined as a sudden decline in the kidneys excretory function, is a common postoperative complication. It is unknown whether preadmission use of ACE-I/ARBs affects the risk of acute kidney injury (AKI) after colorectal cancer (CRC) surgery.

Aim

We assessed the impact of preadmission use of ACE-I/ARBs on the postoperative risk of AKI in patients undergoing surgery for CRC.

Methods

We identified all patients undergoing surgery for CRC between January 1st, 2005 and December 31st, 2014 in Northern Denmark using the Danish Colorectal Cancer Group Database.

Based on reimbursed prescriptions, patients were characterized as current users, former users and non-users (Figure 1).

We assessed the outcome, AKI, using creatinine measurements within seven days after surgery from laboratory data covering all hospitals (Figure 2).

We computed incidence proportions (risk) of AKI with 95% confidence intervals for patients with current, former, or non-use of ACE-I/ARBs, and included death as a competing risk. We compared current, former and non-users of ACE-I/ARB by computing adjusted risk ratios (aRRs) using log-binomial regression. We stratified the analyses of ACE-I/ARB users to address any difference in impact within subgroups.

Figure 2: AKI staging according to Kidney Disease Improving Global Outcomes (KDIGO) criteria.

Stage	Serum creatinine
1	1.5-1.9 times baseline OR ≥ 0.3 mg/dl (≥26.5 µmol/l) increase
2	2.0-2.9 times baseline
3	3.0 times baseline OR Renal replacement therapy OR Increase in serum creatinine to ≥ 4.0mg/dl (≥353.6 µmol/l)[1]

[1]Given the stage 1 criteria ≥ 0.3 mg/dl (≥26.5 µmol/l) increase is met.

Results

The study included 9,932 patients, of whom 21.3% were current users, 6.4% were former users and 72.3% were non-users. The AKI risk for current, former and non-users was 26.4% (95%CI: 24.6-28.3%), 25.2% (95% CI: 21.9-28.6%), and 17.8% (95% CI: 17.0-18.7%), respectively. The aRRs of AKI were 1.20 (95% CI: 1.09-1.32) and 1.16 (95% CI: 1.01-1.34) for current and former users, compared with non-users. The relative risk of AKI was higher in current users with hypertension than in current users without hypertension.

Acknowledgements

PROCRIN has supported the project. The private foundation "Linexfonden" has supported the project with 5.000 DKK.
The Health Research Fund of Central Denmark Region has supported the project with 637.000 DKK

Conflict of interests

The authors have nothing to declare.

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Conclusion

- One in five CRC surgery patients is currently treated with ACE-I/ARB.
- Users of ACE-I/ARB, in particular hypertensive patients, are at increased risk of postoperative AKI

Figure 1
Exposure definition

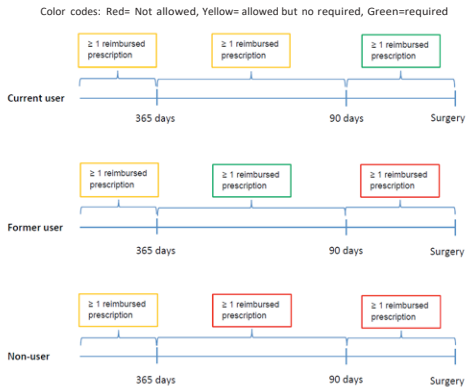

Figure 3
Databases

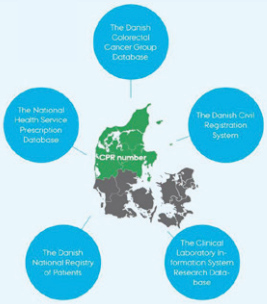

Table 1: AKI risk outcomes (according to ACE-I/ARB user status)

	No. of outcomes	7-day AKI risk % (95% CI)	Crude RR (95% CI)	Adjusted RR[1] (95% CI)
ACE/ARB				
Non-user	1281	17.8 (17.0-18.7)	Ref.	Ref.
Former user	161	25.2 (21.9-28.6)	1.41 (1.22-1.63)	1.16 (1.01-1.19)
Current user	558	26.4 (24.5-28.3)	1.48 (1.36-1.61)	1.20 (1.09-1.32)

[1] Log-binomial regression adjusted for: age (0-59,60-69, 70-79, ≥80), sex, tobacco use, alcohol and BMI, chronic kidney disease, diabetes, heart disease, liver disease, obstructive pulmonary disease, hypertension, cancer type, and urgency of surgery.

SDU NEWS

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EXPOSURE TO PHTHALATE-CONTAINING PRESCRIPTION DRUGS AND THE RISK OF COLORECTAL ADENOCARCINOMA

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Danish users of phthalate-containing drug products (cumulative use ≥ 500 mg) were 11% less likely to develop colorectal adenocarcinomas during 2004-2016 compared to non-users (OR = 0.89; 95% CI: 0.81, 0.96). However, this finding likely reflected confounding from NSAID-use, which by itself is protective against colorectal cancer. When NSAID-users were omitted from the analysis, an increased risk of colorectal adenocarcinomas was seen with phthalate exposure (OR = 1.26; 95% CI: 1.05, 1.51). NSAID-products comprimised 14.7% of diethyl phthalate exposure and 0.9% of dibutyl phtalate exposure.

illustrated by Marie S.

Overset kolorektal cancer ved koloskopi

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Karen Lindorff-Larsen, Nordsim: Færdighedstræning og Simulation, Aalborg Universitetshospital — Christian Torp-Pedersen, Institut for Medicin og Sundhedsteknologi, Aalborg Universit — Charlotte Green Carlsen, Akutafdeling, Aarhus Universitetshospital

Introduktion

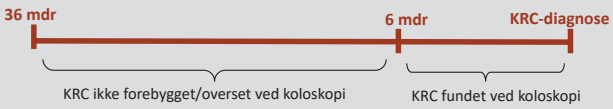
- Koloskopi (kikkertundersøgelse af tyktarmen) er golden standard til diagnostik af kolorektal cancer (KRC) og til fjernelse af polypper (adenomer, som er forstadier til KRC).
- Internationale undersøgelser har dokumenteret en høj rate af oversete KRC. Formålet er at undersøge:

1) Hvor mange KRC der overses ved koloskopi i DK.

2) Hvilke risikofaktorer, der har betydning for at overse KRC.

Metode

- Alle patienter, der har fået foretaget koloskopi i 2001-2012 samt alle patienter med KRC i 2001-2015, blev identificeret fra nationale patientregistre.
- Overset KRC er defineret som min. én koloskopi 6-36 mdr før KRC i overenstemmelse med international konsensus:[1]



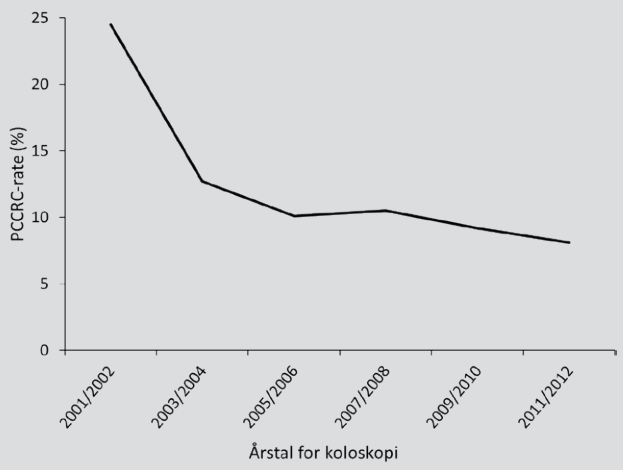
- Risikofaktorer for at overse KRC blev identificeret ved multivariat poisson regressionsanalyse[2].

Resultater

- Vi identificerede 15.419 patienter med mindst én koloskopi og efterfølgende KRC indenfor 3 år.
- 1.382 havde mindst én koloskopi i perioden 6-36 mdr før KRC-diagnose.
- 9,0% af KRC er således overset / ikke-forebygget.

...Én ud af 11 kolorektal cancere blev overset eller kunne potentielt være forebygget...

Andel af oversete KRC over tid:[2]



Risikofaktorer for at overse KRC i DK:

	Relativ Risiko	95% CI	p-værdi
Lokalisation af KRC			
Rektum / Sigmoideum	1,00		
V. fleksur + colon desc.	1,23	0,93-1,61	0,14
Transversum	1,57	1,28-1,93	< 0,001
Højre side	1,85	1,64-2,08	< 0,001
Colon, uspecificeret	2,10	1,76-2,51	< 0,001
Colitits Ulcerosa			
Nej	1,00		
Ja	3,44	2,79-4,23	< 0,001
Disp. arvelig KRC			
Nej	1,00		
Ja	5,32	4,32-6,55	< 0,001
Divertikulit			
Nej	1,00		
Ja	3,22	2,85-3,63	< 0,001

Konklusion

- **Andelen af oversete KRC falder over tid fra 2001 til 2012.**
- **Følgende sygdomme giver øget risiko for at overse KRC:**
  - Arvelig disponering for KRC
  - Colitis Ulcerosa
  - Divertikulit
  - KRC i colon transversum og højre side af colon

Perspektivering

- **75 - 86% af oversete KRC tilfælde kan måske undgås**
  ~ ca. 125 KRC-tilfælde pr år i Danmark[3,4]
- **Uddannelse og kvalitetssikring af koloskopi kan måske nedbringe andelen af oversete KRC.**

1) Morris EJA et al. - Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service. *Gut.* 2015;64(8):1248-1256.
2) Forsberg A et al. - Post-colonoscopy colorectal cancers in Sweden. *Eur J Gastroenterol Hepatol.* 2017;29(7):855-860.
3) le Clercq CMC et al. - Postcolonoscopy colorectal cancers are preventable: a population-based study. *Gut.* 2014;63(6):957-963.
4) Robertson DJ et al. - Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. *Gut.* 2014;63(6):949-956.

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Hvorfor giver studier så forskellige bud på mængde af overdiagnostik

IJC
International Journal of Cancer

As you like it: How the same data can support manifold views of overdiagnosis in breast cancer screening

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Introduktion

Estimater for mængde af overdiagnostik varierer fra 1% til 50% i forskellige studier. Dette har skabt megen diskusion blandt fagfolk og forvirring for borgerne. For at belyse hvor meget valg af studie design påvirker estimaterne, genbrugte vi studie designs fra 6 studier på data fra én population.

Metode

Ud fra følgende kriterier identificerede vi 5 høj-estimat studier:

- Observationelle studier fra rutine screening
- ≥20% overdiagnostik
- estimerede et evt. compensatory drop vhja kvinder over screenings alderen

Et cohort studie fra Fyns Amt har tidligere estimeret ca. 1% overdiagnostik. I studiet blev inviterede kvinder fulgt op til 14 år efter screeningen sluttede. Vhja. Nordcan data for Fyns Amt genskabte vi studie designet fra de 5 høj-estimat studier. De valgte studier viste 25–54% overdiagnostik.

Resultat

Resultater fra de 5 høj-estimat studier og brugen af deres studie design på Fyn populationen.

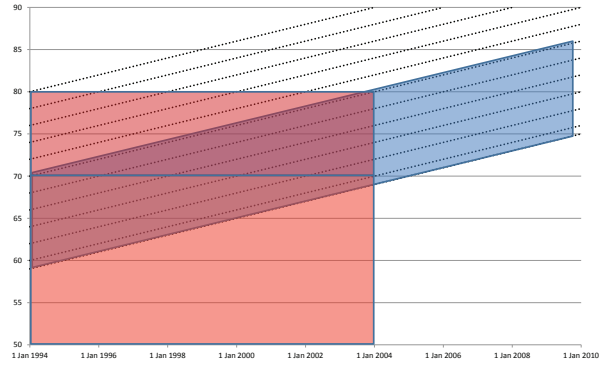
Studie	Land	Overdiagnostik estimat i studiet	Overdiagnostik estimat Fyn, med samme studie design
Zahl et al. 2004[1]	a) Norway b) Sweden	a) 54% b) 45%	a) 56% b) 83%
Jørgensen and Gøtzsche 2009[2]	a) United Kingdom b) Canada c) Australia d) Sweden e) Norway	Overall (meta-analysis):52%	Last pre-screening year: 40% Last year before abrupt incidence increase: 55%
Jørgensen et al. 2009[3]	Funen + Copenhagen	31%[a]	27%[a]
Zahl and Mæhlen 2012[4]	Norway	50%	42%
Kalager et al. 2012[5]	Norway	25% (any follow-up) 18% (10 years of follow-up)	52% (2 years follow-up) 21% (6 years follow-up) 13% (10 years follow-up)
Njor et al. 2013[6]	Funen	1%	1%

Resultat (fortsat)

Reanalysen gav overdiagnostik estimater på 13-83 %, hvilket var bemærkelsesværdig tæt på de oprindelige estimater (table 1). Nærmere analyser viste at:

- overdiagnosis estimaterne blev mere end halverede når baggrunds risikoen (incidensen under screening) blev estimeret mere korrekt
- og faldt yderligere når man ekskluderede fødsels cohorter der aldrig har været inviteret til brystkræft screening fra analyserne.

Comparing study designs in low- and high-estimate studies



Konklusion

De samme data kan give meget varierende bud på over-diagnostik – det hele afhænger af studie designet. En fælles enighed om brugbare epidemiologiske metoder kunne undgå misvisende resultater. Dette studie viser at man i fremtidige studier af overdiagnostik bør sikre at baggrundsrisikoen estimeres korrekt samt at det compensatorisk drop estimeres ud fra en informativ population.

DBCG DANISH BREAST CANCER GROUP

Localization of loco-regional recurrences after neoadjuvant treatment for locally advanced and inflammatory breast cancer

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Purpose

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 recently been published. The purpose of this study is to determine whether these guidelines are appropriate for use in LABC and IBC.

Materials and methods

A total of 202 consecutive patients have been treated for LABC and IBC at our institution from September 2006 to May 2017. Median follow up time was 46 months. Patients were identified by chemotherapy prescription lists and verified by review of treatment records. All patients received neoadjuvant taxane-containing chemotherapy as well as HER-2 targeted and hormone therapy where appropriate. Patients with pathologically verified LRR were identified by review of treatment records. Localization of LRR was determined from records, including clinical photography, imaging studies and radiation therapy treatment plans and charted in accordance with the ESTRO consensus guidelines for early breast cancer. Both patients with LRR as first recurrence, as well as patients developing LRR after distant metastases were included.

Results

Fifteen LRRs were identified in 14 patients. The locations of LRRs are shown in relation to the ESTRO consensus guidelines in figure 1. One patient developed simultaneous LRR locally and in CTVn_L2 while one patient developed an isolated regional recurrence in CTVn_L4. The remaining 12 LRRs were isolated chest wall recurrences. One recurrence was located to the contralateral side of the sternum, thus outside of the mediolateral and craniocaudal boundaries of the CTVp_thoraxwall.

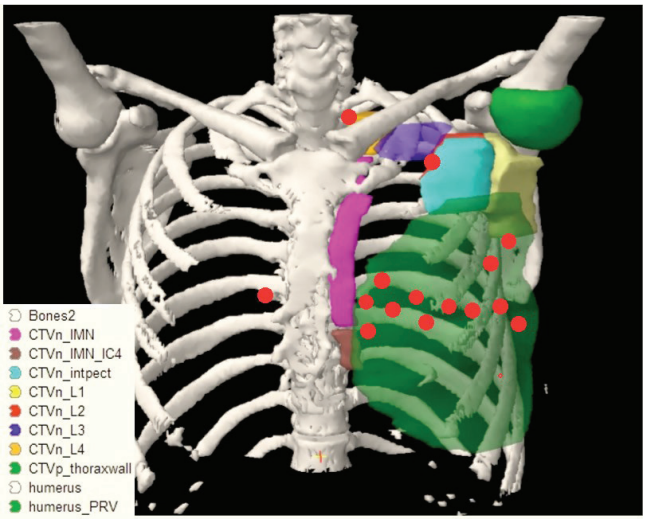


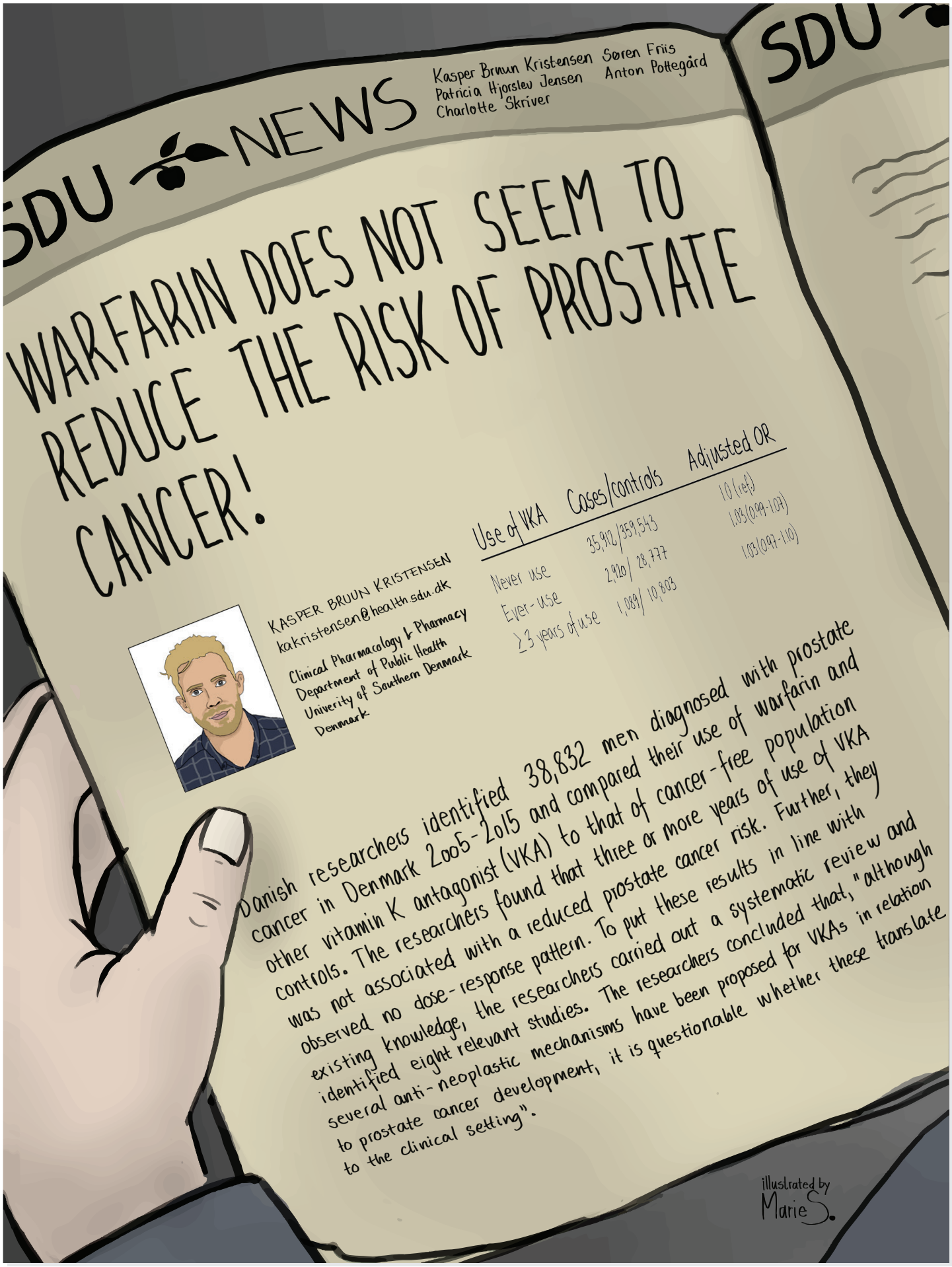
Figure 1: Localization of LRR. Each red dot represents a LRR.

The remaining chest wall recurrences were well within the mediolateral and craniocaudal boundaries. They were characterized by being localized close (less than 1 cm) to the mastectomy scar (12/13) and presenting with skin involvement (11/13). ESTRO consensus guidelines defines the ventral border of CTVp_thoraxwall 5 mm under skin surface and suggests applying a bolus to the mastectomy scar in high risk mastectomized patients. The high frequency of skin involvement underlines the importance of this practice.
One patient with chest wall recurrence had suspicion of metastases in the pectoralis muscles on diagnostic CT, however this was not verified pathologically.

Conclusion

LRRs in LABC and IBC are predominantly located on the chest wall near the mastectomy scar. Due to the high frequency of skin involvement in chest wall recurrences, it should be recommended to apply a bolus to the mastectomy scar during postoperative radiation therapy. With the application of a bolus, use of the ESTRO consensus guidelines would ensure coverage of all but one recurrence, which was located to the contralateral side of the chest wall.

CIRRO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SDU
WARFARIN DOES NOT SEEM TO REDUCE THE RISK OF PROSTATE CANCER!
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Denmark
Use of VKA | Cases/controls | Adjusted OR
Never use | 35,912/359,543 | 1.0 (ref)
Ever-use | 2,920/28,777 | 1.03 (0.99-1.07)
≥ 3 years of use | 1,089/10,803 | 1.03 (0.97-1.10)
Danish researchers identified 38,832 men diagnosed with prostate cancer in Denmark 2005-2015 and compared their use of warfarin and other vitamin K antagonist (VKA) to that of cancer-free population controls. The researchers found that three or more years of use of VKA was not associated with a reduced prostate cancer risk. Further, they observed no dose-response pattern. To put these results in line with existing knowledge, the researchers carried out a systematic review and identified eight relevant studies. The researchers concluded that, "although several anti-neoplastic mechanisms have been proposed for VKAs in relation to prostate cancer development, it is questionable whether these translate to the clinical setting".
illustrated by
Marie S.

Danish Gynaecological Cancer Database – Nursing

Creating evidence for quality improvements in pre- and postoperative cancer care

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INTRODUCTION

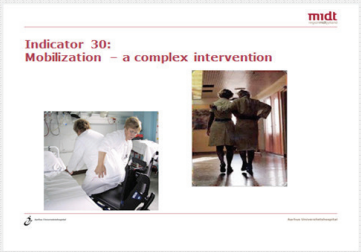
IN GYNAECOLOGICAL CANCER SURGERY, THE QUALITY OF PRE- AND POSTOPERATIVE CARE IS CRUCIAL TO IMPROVE THE OUTCOME AND TO ENSURE THAT COMPLICATIONS OR A POOR GENERAL CONDITION DOES NOT DELAY FURTHER TREATMENT AND RECOVERY

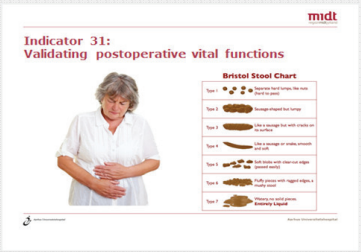
AIM

TO MONITOR THE QUALITY OF PRE- AND POSTOPERATIVE CARE AT NATIONAL LEVEL AND TO GENERATE DATA FOR RESEARCH

MATERIAL AND METHODS

REAL TIME DATA ARE BEING ENTERED BY CLINICAL NURSES AT THE NATIONAL CANCER CENTRES. TO ENSURE THAT CARE DELIVERY IS CONSISTENT AND DOCUMENTED IN PATIENT FILES, CLINICAL CARE RECOMMENDATIONS HAVE BEEN DEVELOPED AND IMPLEMENTED BY LOCAL NURSING REPRESENTATIVES. IN THIS PROCESS, CLINICAL QUALITY INDICATORS ARE USED TO MONITOR THE QUALITY OF CARE.



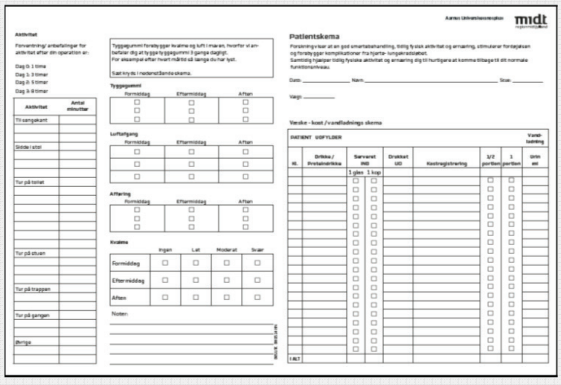


RESULTS

DURING 2011-2017, A NUMBER OF 5726 PATIENTS UNDERGOING SURGERY FOR OVARIAN, ENDOMETRIAL, AND CERVICAL CANCER HAVE BEEN REGISTERED (NATIONAL COVERAGE: 94%). AT PRESENT, 436 DIFFERENT VARIABLES MONITOR CENTRAL PRE- AND POST-OPERATIVE CARE ELEMENTS CONCERNING MOBILISATION, NUTRITIONAL STATUS, PAIN SCORE, VITAL FUNCTIONS, AND PSYCHOSOCIAL SUPPORT.

THE IMPACT OF DGCD NURSING

- OFFERS A COMPREHENSIVE OVERVIEW OF PATIENT PATHWAYS AT NATIONAL LEVEL
- ADDS TO IMPLEMENTATION OF EVIDENCE BASED PRE- AND POSTOPERATIVE CARE
- SUPPORTS FORMATION OF PROFESSIONAL NETWORKS AND DEVELOPMENT
- REPRESENTS A BASIS FOR RESEARCH



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Awareness and surveillance reduces head and neck radiotherapy treatment length

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Purpose / Objective

Treatment course length is important for outcome in radiotherapy of head and neck cancer patients. National guidelines prescribe a maximum course length of 41 days for moderate accelerated treatment (6 fractions/week), and 48 days for non-accelerated treatment (5 fractions/week).

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 and materials

The study included 2,011 head and neck cancer patients treated between 2003 to 2017 to 66-68 Gy in 33-34 fractions and never re-irradiated.

As a part of a National Cancer Plan in 2005, the focus increased on the “Patient pathways in cancer packages”. 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 was checked, and it was ensured that the first treatment was not on a Friday and the last treatment not on a Monday. Patients with scheduled treatment violations, according to national guidelines, are conferred with the responsible oncologist and the treatment plan is compensated with an extra fraction in the last week of treatment.

Conclusion

- Guidelines, capacity and QA-procedures are essential to keep overall treatment time.
- Local procedures are necessary to reduce treatment delays.
- Continuous surveillance eliminates almost all deviations.

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 (fig. 1), 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 DAHANCA guidelines introduced in 2013 to less than 20 % for accelerated treatments and to less than 40 % for the non-accelerated treatments after 2011 (fig. 2).

The introduction of 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 (fig. 2). The surveillance alternates between two radiation therapists and takes approximately 5-15 minutes per week in total for all active treatments.

Fig. 1: Average treatment length

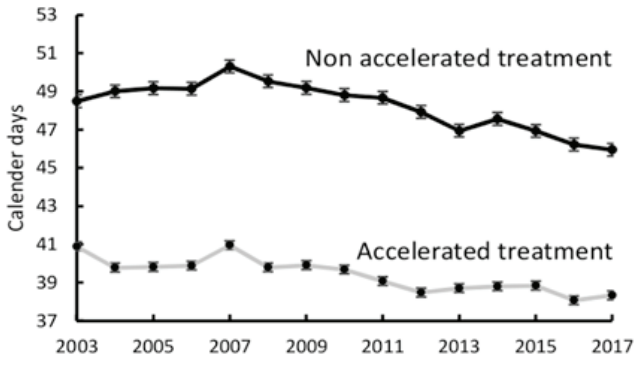
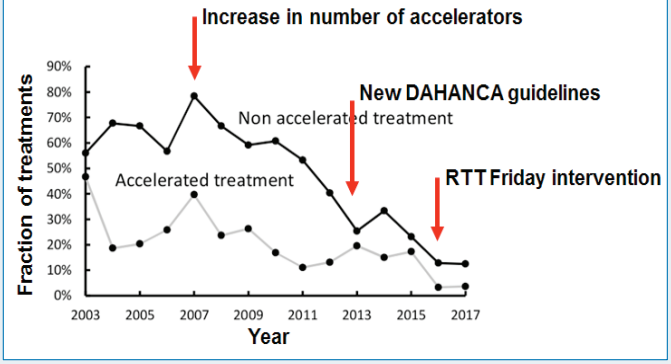


Fig. 2: Deviation (%) in overall treatment time



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