STENO DIABETES CENTER ODENSE (SDCO) PHD FUND
Layman descriptions for awarded grants

2019

	**Anders Bossel Holst Christensen**	**Department of Ophthalmology**	**Automatic Detection of Diabetic Macular Edema in Optical Coherence Tomography Images Using Artificial Intelligence**	**2nd round 2019**

Diabetes is one of the most challenging diseases of our time. In 2017, 451 million people worldwide had diabetes, and this number is expected to increase to 693 million by 2045 [1]. Patients with diabetes are inherently at risk of getting eye complications as a result of their disease. In time, most patients with diabetes will be affected by diabetic retinopathy (DR), which may be complicated by diabetic macular edema (DME) and other sight threatening changes in the retinal vasculature. It is estimated that around 3.8% of patients with diabetes will be affected by DME [5]. DME causes central visual blurring, but timely treatment may reduce the vision loss by up to 90% [7]. In order to detect DME at an early stage, it is essential to perform regular eye screening. Currently, in Denmark eye screenings are performed by fundus photography with manual assessment by trained graders. If DME is suspected, a macular optical coherence tomography scanning (OCT) is performed to increase the diagnostic certainty. At present, this is also manually inspected. The current evaluation method is difficult to evaluate, time-consuming as well as strenuous and, thus, susceptible to human errors due to stress and fatigue. As the number of patients with diabetes is increasing, the workload in relation to making eye screenings is expected to increase considerably.

In this project, we intend to use a branch of artificial intelligence called deep-learning, in which algorithms can be used to build an automatic system for detection of DME in OCT images with the end goal of acting as decision support to determine whether patients should be referred to treatment or not.

Deep learning algorithms have in the recent years, with the technological advancements, become very popular in many sorts of data-related tasks. They can for example be used for recognizing particular patterns or objects in images. By presenting the algorithms with a high number of images with different forms of known disease (for instance DME), the algorithm can “learn” to identify these different forms of disease in yet unseen images. After training the algorithm, it will be possible to deploy it in a practical setting, where it will be able to provide accurate, instantaneous diagnosis, thereby reducing the work load of health care professionals.

At the University of Southern Denmark (SDU), researchers are currently working on a similar system for detecting DR in retinalfundus photography images. Combining these two systems will provide the doctor with a valuable tool for in-depth analysis of retinal images and scans. To achieve our goal, a close collaboration between Odense University Hospital (OUH) and Steno Diabetes Center Odense (SDCO) will ensure the best opportunities for the success of the project.

The proposed study will be divided into three parts. In the first part, in addition to generating the data, a method for grading and annotating the images will be developed. In the second part of the study, the algorithms will be developed and trained to be able to detect DME as present or not in the OCT images and to provide referral decisions. For this task, we will annotate 10.000 OCT images which will be used for training, validation and testing of the networks in an 80/10/10 split. In the third and final part of the project, the trained algorithms will have to be tested in terms of their agreement with human experts, and in terms of their practical usage in the clinic. The performance of the method will be evaluated using accuracy, specificity, sensitivity, AUC, positive- & negative predictive values and a Kappa score as statistical measures.

	**Anne Suhr Thykjær**	**Department of Ophthalmology**	**Diabetic Retinopathy in Response to Systemic Treatment and Intervention - Real World Data From a National Danish Database**	**2nd round 2019**

Diabetic eye disease (DR) is the most common complication in diabetes, and people with diabetes attend yearly eye screenings to track their disease progression and avoid vision loss. The patients are screened by either a private practicing ophthalmologist or at one of the ophthalmology departments at the public Danish hospitals. The screenings involve photos of the retina, at the back of the eye, to determine the severity of the diabetic eye disease. Each year data from approximately 100,000 patients with DR are registered in the Danish Registry of Diabetic retinopathy (DiaBase).

These patients are treated with different drugs to control blood sugar levels, but also drugs against high cholesterol and high blood pressure, if needed. Some of the patients may also have received interventions that are more invasive than regular drug-therapy; such as insulin pumps, that administer insulin automatically, surgery for obesity, bypass operations because of blood clots or to avoid these, in the patients' heart.

In the present project we aim to build a data collection by integrating DiaBase with other national Danish databases that include data on disease, treatment and medications. We want to validate the quality of data from DiaBase by inviting 250 patients to a new clinical examination with the best available diagnostic tools. We will also to conduct analyses of the collected data and investigate if specific diabetes-related drugs as well as the other aforementioned drug-groups and surgical interventions may be beneficial or harmful to the eye in relation to diabetic eye disease.

The data in Diabase has never been validated. The input is based upon different levels of expertise and methods of imaging. This study will ensure that the quality of the reported data is sufficient, by inviting patients who recently has had their eyes screened, to a new, state of the art examination, with the newest imaging technology.

By connecting the validated data from the Diabase with registries of disease, treatment and medications, it will be possible, not only in this study, but in many future studies, to use the data to make potential connections between diabetic eye disease, its progression and development, and different drugs or interventions. This will potentially better our understanding of diabetic eye disease and in relation to the treatment of diabetes, high blood pressure, high cholesterol etc., which essentially might lead to optimized treatment and prevention of blindness.

	**Kristoffer Jensen Kolnes**	**Steno Diabetes Center Odense (SDCO)**	**Adipose tissue dysfunction in type 2 diabetes and its reversibility by gastric bypass and exercise**	**2nd round 2019**

BAGGRUND

Insulinresistens spiller en afgørende rolle i udviklingen af type 2 diabetes og for den øgede risiko for hjertekarsygdom, man ser ved denne sygdom. På trods af mange års forskning er det endnu ikke lykkedes at udvikle en målrettet behandling af insulinresistens bortset fra vægttab og øget fysisk aktivitet. Det kan måske forklare, hvorfor en behandling som nedbringer blodsukrene (glykæmisk kontrol) med de diabetespræparater som findes på markedet i dag ikke har den store effekt på risiko for hjertekarsygdom og død. Forskningen viser i stigende grad at såkaldt fedtvævsdysfunktion, og især en nedsat evne til at udvide (ekspandere) fedtvævet, spiller en betydelig rolle for fedme-relateret insulinresistens. Men hvilken rolle det spiller i udviklingen af type 2 diabetes - som jo er karakteriseret ved både insulinresistens og nedsat insulinsekretion - mangler i høj grad at blive belyst.

FORMÅL

Hovedformålene med vores projekt er at undersøge hypoteserne:

1) At såvel helkrops som muskulær insulinresistens hos patienter med type 2 diabetes er forbundet med en forværret grad af fedtvævsdysfunktion end det man ser ved fedme alene
2) At den forbedrede insulinfølsomhed der opnås efter fedmeoperation (gastric bypass) hos patienter med type 2 diabetes i høj grad kan forklares ved en forbedret fedtvævsfunktion og evne til fedtvævsekspansion.
3) At den positive effekt af høj intensiv interval træning (HIIT) på insulinresistens og insulinsekretion hos patienter med type 2 diabetes i høj grad kan forklares ved en forbedret fedtvævsfunktion og evne til fedtvævsekspansion.

FORSKNINGSPLAN

Vi vil først undersøge en lang række kendte markører for fedtvævsdysfunktion og samtidigt identificere nye markører for forværret grad af fedtvævsdysfunktion hos patienter med type 2 diabetes sammenlignet med raske personer med fedme eller normal vægt. Vi vil herefter undersøge effekten af henholdsvis fedmeoperation (gastric bypass) og en ny form for træning (HIIT) på både de kendte og de nye markører for fedtvævsdysfunktion hos personer med fedme med og uden type 2 diabetes.

For at undersøge og identificere disse henholdsvis kendte og nye markører vil vi på blodprøver og fedt- og muskelbiopsier anvende avancerede metoder som 1) såkaldt RNA sequencing og qRT-PCR til bestemmelse af gen-ekspression, 2) western blotting til bestemmelse af proteinmængde og aktivitet, 3) plasma- og vævs-metabolomics, samt 4) analyser af adipokiner og myokiner.

Ændringer hos patienter med type 2 diabetes og efter fedmeoperation (gastric bypass) eller træning (HIIT) vil blive relateret til målinger af glukose og fedtmetabolisme, insulinfølsomhed og insulinsekretion samt målinger af markører for insulinresistens i muskelvæv. Yderligere indsigt i mekanismer vil blive opnået ved studier af immortaliserede dyrkede fedtceller opnået fra mennesker.

PERSPEKTIVER
Dette projekt vil give os en ny og vigtig indsigt i sammenhængen mellem fedtvævsdysfunktion og udvikling af type 2 diabetes, og definere i hvilken grad fedmeoperation (gastric bypass) og fysisk træning (HIIT) kan fjerne eller forbedre denne tilstand og dermed forbedre insulinfølsomhed og måske insulinsekretionen hos patienter med type 2 diabetes.

Vi forventer endvidere at vores fund kan anvendes til udviklingen af ny medicin til behandling af insulinresistens, som på nuværende tidspunkt mangler i forebyggelsen og behandlingen af type 2 diabetes og hjertekarsygdom.

	**Anne Sofie Faarvang Thorsen**	**Department of Clinical Biochemistry and Pharmacology**	**The arterial wall in patients with diabetes: Do changes in arterial basement membrane proteins predict future arterial disease? Are remodeling processes altered?**	**1st round 2019**

1.
People living with type 2 diabetes are told that they have a significantly higher risk of developing diseases related to the heart or blood vessels. These diseases can play a major role for the overall health of the patient and can even cause death due to a blood clot in the heart, brain or other parts of the body. Understandably, this information can cause a great deal of stress and anxiety for the patient.

As of today a doctor cannot determine which patient has a higher risk of disease in the heart and blood vessels. Therefore, we see a great need for further exploration of the mechanisms that could help identify diabetic patients with a particularly high risk of developing these diseases.

In this PhD project we aim at identifying diabetic patients with a specific pattern in the amount of proteins in the blood, tissue and genetic material who are at high risk. We explore this problem from two angles.

In the first part of the PhD study, we identify and measure proteins which are related to high risk of disease in the heart and blood vessels. These proteins come from the blood vessels (a specific part called the basement membrane) and are believed to be present in a higher concentration when people have diabetes. At the same time we measure the same proteins in a blood sample from the patients, and we also examine their genetic properties with a focus on specific genetic areas. All the tissue and blood samples have already been collected from patients who (since 2008) have undergone a by-pass operation in the heart at Odense University Hospital . All of the material is stored in a biobank (Odense Artery Biobank). We also collect data from Statictics Denmark concerning stays in hospital, death or other diseases about each individual. These data are used to categorize people into risk categories. We then hope to see a pattern in the measurements from blood and tissue that match the risk profile of the patient.

In the second part of the study we use a different approach. Data from a large study conducted on the population of Malmö, Sweden, can be used to examine the development of blood vessels in diabetic patients.

In this study people from Malmö (some with diabetes) have undergone a number of examinations in the early 1990's and again 15 years later. One of the tests was an ultrasound of the large blood vessel of the neck, the socalled carotid artery. With this ultrasound we are able to measure the thickness of the wall of the blood vessel and the diameter in which the blood can pass through.

We think that there is a connection between diabetes and the diameter of the blood vessel and that, over time, diabetes can cause the blood vessel to become narrower. This idea links the two studies because the same proteins that can be found in the

first study are important in determining the risk of having a narrow blood vessel when the patient suffers from diabetes.

2.
This project can contribute with a deeper knowledge about the linking mechanisms between diabetes and disease in the heart and blood vessels: which proteins are present in higher concentration? How does this relate to a higher risk? How do diabetic blood vessels change over time? We will aim at answering these questions.

We see several perspectives:
- deeper knowledge and understanding of the mechanisms behind disease in the heart and blood vessels that follows diabetes
- development of a new blood test. Over time, the proteins measured in this study could be developed to a new blood test that gives information about a patient's risk of developing a disease in the heart or blood vessels
- better treatment for patients with diabetes because a patient with high risk can be treated more intensely

3.
In order to achieve the goals of this project there are several overall tasks:
- select patients form the biobank that are suitable for the project (the correct type of tissue and blood sample available)
- analyze blood and arterial tissue in the laboratory. This includes cutting and preparing tissue and analyzing the tissue and blood samples.
- collect data form Statistics Denmark. This process can be quite detailed and time consuming.
- obtain data from 'The Diet and Cancer Study' in Sweden, Malmö - analyze data from study 1
- analyze data from study 2
- write articles - finally, collect all parts of the project together

	**Martin de Almeida**	**Department of Sports Science and Clinical Biomechanics**	**High-intensity interval training combining rowing and cycling: effects on muscle lipid droplet localization and perilipin interactions in health and type 2-diabetes**	**1st round 2019**

Diabetes er en af de største nationale sundhedsudfordringer. Næsten 6% af den danske population er diagnosticeret med diabetes, hvilket er estimeret til at fordobles over de næste 10 år. Type 2-diabetes (T2D) udgør ca. 80% af tilfældene, er tæt forbundet med overvægt og inaktivitet, og er karakteriseret ved en nedsat følsomhed i cellerne for insulin (insulin resistens; IR). Nyere forskning påviser, at indholdet og placeringen af lagrede fedtsyrer (lipid dråber; LD) i skeletmuskulaturen er forbundet med insulinfølsomheden. Imidlertid eksisterer der sparsom viden om de cellulære mekanismer bag, og hvordan muskel LD påvirkes af akut/længerevarende træning.

Den centrale hypotese i projektet er, at afvigelser i den fedtsyrespecifikke placering i muskelcellen kan forklare udviklingen af IR, som det ses ved et kalorieoverforbrug og forbedringerne efter træning. Derudover vil projektet undersøge effekterne af 8 ugers høj-intens intervaltræning (HIIT) på disse muskelegenskaber og forbindelsen til IR hos T2D patienter og raske deltagere. Foreløbige data viser betydelige træningseffekter med 43% stigning i insulinfølsomheden, såvel som forbedringer i kondition, kropskomposition og langtidsblodsukker.

Projektet vil forbedre vores forståelse af den grundlæggende cellefunktion og hvilken rolle LD-metabolismen har for skeletmuskulaturens insulinfølsomhed. Dette vil danne basis for mere effektive træningsstrategier og udviklingen af forebyggende medicin, der lindrer og muligvis forhindrer T2D.

	**Massar Omar**	**Department of Cardiology**	**Effect of empagliflozin on left ventricular function and hemodynamics at rest and during exercise in patients with heart failure and with reduced ejection fraction. A randomised clinical trial**	**1st round 2019**

Hjertesygdomme er trods forbedringer i forebyggelse og behandling fortsat forbundet med betydelig sygelighed og dødelighed. I slutfasen af hjertesygdom vil hjertets pumpekraft svækkes, og patienterne vil udvikle hjertesvigt, som er forbundet med betydelig reduceret livskvalitet og høj dødelighed.

Behandlingen af hjertesvigt er baseret på kombination af medicin, som hæmmer overaktivering af flere hormonsystemer. I en

undersøgelse, hvor sikkerheden af en ny type medicin til behandling af sukkersyge (Empagliflozin) blev undersøgt, fandtes en overraskende gavnlig effekt af sukkersygemedicinen hos patienter med hjertesvigt. Undersøgelserne var planlagt til at undersøge, om medicinen var sikker på patienter med sukkersyge og hjertekarsygdomme og var derfor ikke designet til at belyse virkningsmekanismer for effekten.

Den aktuelle undersøgelse sker i samarbejde mellem OUH, Rigshospitalet og Herlev Gentofte hospital og skal afklare virkningsmekanismen af den nye type sukkersygemedicin på hjertet og kredsløb hos patienter med kendt hjertesvigt. Effekten belyses ved at undersøge blodkoncentrationer af hormonstoffer, som udskilles af det svigtende hjerte ved avanceret ultralydsskanning af hjertet og ved avancerede kredsløbsundersøgelser med direkte måling af blodtryk og minutvolumen i lungekredsløbet.

Hovedformålet er at undersøge effekten af tre måneders behandling med Empagliflozin 10 mg dagligt eller placebo på koncentrationen af hjerte-biomarkøren NT-proBNP hos 189 stabile, symptomatiske hjertesvigtspatienter med nedsat pumpefunktion af venstre hjertekammer.

Patienter inkluderet på OUH får foretaget avanceret kredsløbsmåling med direkte måling af lungeblodtryk og minutvolumen i hvile og under fysisk belasting før og efter 3 måneders behandling med Empagliflozin 10 mg daglig (højspecialiseret undersøgelse).

Yderligere anvendes avanceret hjerteultralyd til at undersøge funktionen af det venstre hjertekammer; sukkeromsætningen, ketonstof i blodet og nyrefunktion undersøges.

Endelig vil effekten af medicinen på patienternes fysiske aktivitet blive bedømt vha. patientbåret accelerometer og specifikke livskvalitets spørgeskemaer udviklet til hjertesvigtspatienter.

Betydning
Dette projekt vil biddrage med vigtig information om funktion af medicinen på størrelse og funktion af venstre hjertekammer og kæde det sammen med den enkelte patients daglige aktivitetsniveau og livskvalitet. Ydermere vil forsøget biddrage med unik information om den hæmodynamiske (kredsløbs) virkninger af Empagliflozin i patienter med hjertesvigt under hvile og under belastning.

På sigt er håbet at kunne bruge præparatet i behandlingen af patienter med hjertesvigt og derved øge patients overlevelse, hjertets funktion samt livskvalitet. Resultatet af undersøgelsen forventes offentliggjort i internationale videnskabelige tidskrifter.

Metode
Patienter rekrutteres fra hjertesvigtsambulatorierne på de deltagende hospitaler. Patienterne rekrutteres på Rigshospitalet, Herlev-Gentofte Universitetshospital eller Odense Universitetshospital. Efter der er indhentet informeret samtykke foretages fysisk undersøgelse, blodprøver, urinprøver, foretages sukkerbelastningstest, ultralydsscanning af hjertet i hvile, påsætning af accelerometer og vurdering af nyrefunktion og måling af hjertespecifikke hormonstoffer. Patienter inkluderet På Odense Universitetshospital vil yderligere få foretaget belastnings undersøgelse efter anlæggelse af trykkateter i lunge kredsløbet. Når undersøgelser er foretaget trækkes lod om aktiv behandling eller behandling med placebo (uvirksom tablet). Undersøgelsen er blindet så hverken patient eller læge kender behandlingen. Efter 3 måneders behandling gentages alle undersøgelserne. Når studiet er afsluttet sammenlignes de 2 grupper.

Projektet er forankret på Hjertemedicinsk Afdeling OUH, Hjertemedicinsk klinik B Rigshospitalet og Hjertemedicinsk afdeling Herlev Gentofte hospital. Professor Jacob Eifer Møller OUH, overlæge Lars Videbaek OUH, professor Finn Gustaffson og overlæge Morten Schou er akademisk ansvarlig for projektet. Dataindsamling, inklusion af patienter, randomisering og undersøgelse af patienter varetages af Ph.d. studerende, Massar Omar (OUH) og Jesper Jensen (Herlev). Undersøgelsen er igangsat af forskergruppen uafhængigt af fabrikanten af Empagliflozin og er delvist støttet økonomisk af Hjerteforeningen.

2018

	**Jakob Andersen**	**Department of Ophthalmology**	**Automatic Screening of Diabetic Retinopathy by Artificial Intelligence**	**1st round 2019**

Diabetic eye disease (diabetic retinopathy, DR) is a severe complication among patients with diabetes and the leading cause of blindness in people of the working-age. In time, DR will affect most patients with diabetes, and it may lead to sight-threatening

changes of the retinal vasculature. Fortunately, the disease is manageable, and in fact 90% of cases of severe vision impairments are preventable if detected in time. Therefore, it is important for patients with diabetes to attend regular eye screening in order to detect sight-threatening DR before potentially irreversible vision loss occurs.

Currently, screening for DR involves regular caption of retinal photographs which are then evaluated manually by human experts. The current evaluation method is time-consuming as well as strenuous and, thus, susceptible to human errors due to stress and fatigue. In addition, the number of people with diabetes is increasing in Denmark and worldwide, which will increase the demand for eye screenings in the years to come. In this project, we intend to use a recent advancement in computer science called deep-learning as the main building block in an automatic DR screening system. Deep-learning algorithms can be used for image recognition based on the principle that the computer is presented to a high number of images with different forms of a known disease (for instance DR). The algorithm will then "learn" to diagnose the disease. Deep-learning have recently been used for automatic grading of DR, yielding results comparable to human experts.

However, there is an important limitation to this method known as the "black box". That is, that the algorithm only gives a specific diagnosis but is not able to tell how this was achieved (i.e. what is inside the black box). This has led to some concern that the algorithms may give inaccurate diagnoses. Newly developed deep-learning algorithms allow for a look into this black box. This specific type of deep-learning can be used to classify individual image elements (pixels) and can thus be used to extract the same features used by experts to determine disease severity. The use of computers for automatic detection of DR has been an area of active research for many years, but up until the advent of deep-learning, these methods have failed to achieve adequate diagnostic quality.

We believe the method proposed in this study has the potential to improve the quality and effectiveness of DR screening compared to the manual screening methods currently used, as well as the automatic screening methods previously proposed. Currently, due to the amounts of screenings and the use of a manual screening procedure, patients can expect to wait weeks before they are given the result of their screening. Such a long waiting time can be both frustrating and potentially harmful due to undiagnosed sight-threatening changes in the eyes of patients. If successful, our proposed method would be able to deliver an almost instant diagnosis. This would decrease waiting times for patients and the work load on doctors, likely resulting in fewer cases of DR related blindness. To achieve our goal, we will use the imaging systems already used at Odense University Hospital (OUH) to capture images used for training of our algorithm. Hence, it will be possible to implement the new system directly in the screening of DR at OUH, and, furthermore, it will be possible to develop the program continuously after it has been implemented.

The proposed study will be divided into two main parts. In the first part of the study, we will train an algorithm based on 200 expert-graded retinas from OUH. In order to comply with the quality of screening at OUH and "Fyns Diabetes Database" we will capture six "fields" for each retina included in the study, meaning six images are captured per retina. Based on previous work on deep-learning and DR detection, we estimate that upwards of 60.000 images are needed for training of deep-learning algorithms for this particular task. We will therefore make use of data augmentation, which is widely and succefully used in the context of deep-learning to increase the number images avialiable for training and we have in a recent pilot study confirmed the effectivenes of this method. In the second part of the study, we will use 250 retinas of different levels of DR from OUH to test the algorithm against two retinal experts in order to validate the accuracy of the algorithm.

Encouraging results of using deep-learning for extraction of DR features were recently achieved by our group and described in the paper "Using Fully Convolutional Neural Networks for Semantic Segmentation & Automatic Extraction of Diabetic Retinopathy Features in Retinal Fundus Photographies". I will present these results at the upcoming annual meeting of the Association for Research in Vision and Opthalmology.

	**Louise Laage Stentebjerg**	**Department of Surgery**	**The effect of gastric bypass surgery on glucose metabolism, gestational weight gain and fetal growth in subsequent pregnancy**	**1st round 2019**

Background

In Denmark, at least 5000 gastric bypass operations has been performed the last decade. Gastric bypass causes reduced appetite, malabsorption and altered release of important hormones from the intestines. This is useful for loosing weight, but can lead to complications during pregnancy. Among others, these complications comprise low blood sugar and affected fetal growth. Low blood sugar usually does not occur until one year post surgery and evolves gradually with non-specific symptoms, causing delayed diagnosis. Pregnancy aggravates the tendency to get low blood sugar. Thus, the pregnant women with previous gastric bypass are in particular risk. Symptoms of low blood sugar counts: lightheadedness, sweating, confusion, difficulty concentrating, loss of consciousness etc., and can lead to reduced quality of life. In addition, these women often have difficulty absorbing iron and

vitamins. In theory, iron and vitamin deficiency, low blood sugar and a continued weight loss during pregnancy can compromise the growth and development of the fetus. Both over- and under-nutrition in pregnancy have severe consequences for the growth of the fetus and health in later life. Data from our own clinic at OUH show that 40% of women with previous gastric bypass fail to gain the recommended amount of weight during pregnancy.

Aims
The planned PhD study is collaboration between Odense University Hospital (OUH) and Sydvestjysk Sygehus (SVS) and is intended to conduct thorough examinations of blood sugar and hormonal response, trimester-specific occurrence of low blood sugar after meals and fetal growth.

Participants
20 pregnant women with previous gastric bypass will be compared to 20 pregnant women, who have had the same number of children earlier, have the same age and the same body mass index (BMI) previous to their pregnancy.

Methods
Low blood sugar Blood sugar levels during everyday life will be assessed in each trimester and 4-6 weeks following childbirth with a sensor inserted into the skin. The glucose sensor is injected under the skin – an ordinary method used in patients with diabetes that is not painful. The sensor will measure blood sugar levels in 6 days. During these days, the pregnant women report any symptoms of low blood sugar. Twice during pregnancy (in pregnancy week 12-14 and 34) the pregnant women will perform a 4-hour liquid meal test with ingestion of a liquid meal and concomitant measurements of blood sugar-, insulin- and other hormone levels. Information on time for gastric bypass, weight trajectories (before gastric bypass, before, during and after pregnancy), complications related to surgery and pregnancy, blood pressure etc. will be gathered.

Fetal growth
In pregnancy week 24, 28 and 34 ultrasounds will be performed measuring the fetal weight and abdominal circumference. Within 72 hours from the birth of the child a DXA-scan (measuring body fat) and measurements of birthweight, length, abdominal circumference and skinfolds will be performed. Adverse effects, risks, complications and disadvantages All participants will have blood drawn and a sensor injected under the skin. This is not associated with pain, but for some discomfort. DXA-scans will be performed, when the newborn has fallen asleep after breastfeeding/formula feeding. The examination will last for about 5 minutes and is not associated with any pain or discomfort. The exposure of radiation is negligible and poses no risk for the newborn.

Perspectives
Recently, the requirements to be a candidate for gastric bypass surgery have been eased up. Therefore an increase in the number of operations performed is expected. A better understanding of blood sugar and related hormones and fetal growth in women with previous gastric bypass surgery will support risk assessment and development of treatments both before and during pregnancy. Knowledge about the growth of the fetus is important to guide these women towards the most appropriate time for conceiving after gastric bypass surgery. The treatment and follow-up of these patients in the Region of Southern Denmark takes place at OUH and SVS. Research collaboration in this new area will support the development of the functions in the Region of Southern Denmark.