Master Projects
Clinical Physics

December 2018
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1 Projects at Maxima Medical Center, Veldhoven

MMC is a large education hospital in the region of Eindhoven and is one of the 10 centers in the Netherlands (8 of them are the academic centers) that has a Neonatal Intensive Care Department (NICU). Since many patients at the NICU are prematurely born children, the women that are at risk for delivering prematurely are also in MMC cared for at an Obstetric High Care Unit. Thus, the continuum of care around birth and in particular for patients requiring intensive care is arranged in MMC in a high-tech environment.

Clinical Physics in Maxima Medical Center has a research group, in which on average 3-4 students are simultaneously working on their traineeship, Master or PhD project. The research focus of this group has been on signal analysis and image processing in clinical practice, mainly focusing on the two main research topics in MMC: 1) Mother-and-Child Care, 2) Prevention and rehabilitation.

1.1 Improvement of ventilation therapy by early detection of pulmonary deterioration.

Contact: Carola van Pul c.v.pul@tue.nl (clinical physicist)

Background: Advances in antenatal, perinatal, and neonatal care have led to improved survival rates for preterm infants. These infants usually require intensive care at a NICU and are often ventilated mechanically. These vulnerable premature infants stay in an incubator, and their vital signs are continuously monitored in order to detect the patient’s status. Automatic ventilation therapy is currently in development, however the effects of automation are not well-known yet. Furthermore, instability in the situation can result in deterioration. This project will focus on evaluation of automatic ventilation with focus on improved detection of pulmonary deterioration.

Objectives:
1. To evaluate the current automatic ventilation and compare this to conventional ventilation (part of a clinical study)
2. To develop an algorithm to improve the detection of pulmonary deterioration and in particular apnea.
3. To develop a model investigating the coupling between cardiac and respiration rhythm in order to support the detection algorithm.

Study design: Part of a prospective clinical study on the ventilation therapy, conducted in multiple sites. Data collection has been started in 2017 and first datasets are available. First exploration of the data will be performed, and in combination with developing a model, the algorithm will be developed.

Student background: Master student in electrical engineering, biomedical engineering or physics.

Duration: 9-12 months

Student skills: Matlab (or Mathematica) programming, data analytics, modeling, signal processing and willingness to understand neonatal physiology.

Location: Maxima Medical Center, Veldhoven.

Involved supervisors: Hendrik Niemarkt (neonatologist), Peter Andriessen (neonatologist); Carola van Pul (clinical physicist); Ward Cottaar (professor Applied Physics).

1.2 Oxygen saturation after birth as parameter for detection of patent ductus arteriosus

Contact: Carola van Pul c.v.pul@tue.nl (clinical physicist)

Background: In fetal life, an artery called the ductus arteriosus connects the pulmonary trunk to the aortic arch, shunting blood past the lungs and the left ventricle. After birth, the ductus closes within 24-48 hours, ensuring that the blood passes through the lungs and the left ventricle. In approximately 30% of the preterm infants with a birthweight lower than 1500 g, the ductus arteriosus fails to close after birth, resulting in a patent ductus arteriosus (PDA). A significant PDA results in blood shunting from the right ventricle to the aorta (lower oxygenation), or from the aorta to the right ventricle (lower functional output to the peripheral system, pulmonary overload). Initially, this results in a subclinical stage where no or few clinical signs can be seen, as the effect of the ductal steal is well compensated and hard to notice without an echocardiogram. However, without closure, this may eventually result in pulmonary edema, necrotizing enterocolitis and more. Therefore, it is important to diagnose and treat a PDA in an early stage. One important parameter may be the oxygen saturation, which will increase after birth promotes ductal closure.
Objectives:

1. We aim to establish a multitude of parameters which indicate if a PDA is present in a patient, one of them being the oxygen saturation. This can range from simple mean oxygen saturation values over certain windows to more complex methods; this is for the student to decide.

2. In order to better understand the maturation and ductal closure processes, a mathematical model can be used. To determine the parameters in this model, additional ultrasound and blood pressure measurements are needed.

Study design: Observational study based on available data. Regression analysis will be used to investigate the effect and the extent of these variables and further data mining techniques will be explored.

Student background: Master student in electrical engineering, biomedical engineering or physics.

Duration: 9-12 months

Student skills: Matlab (or Mathematica) programming, data analytics, modeling, signal processing and willingness to understand neonatal physiology.

Location: Maxima Medical Center, Veldhoven.

Involved supervisors: Frank Bennis (PhD student); Peter Andriessen (neonatologist); Carola van Pul (clinical physicist); Peter Bovendeerd (biomedical engineering); Ward Cottaar (professor Applied Physics).

1.3 Heart Rate Variability in Preterm Infants upon sepsis

Contact: Carola van Pul c.v.pul@tue.nl (clinical physicist)

Background: Sepsis is a life-threatening condition for neonates that arises when the body's response to infection injures its own tissues and organs. However detection based on conventional clinical patient monitoring is not straightforward. The phenomenon of heart rate variability (HRV) provides physiological insight into regulatory changes and might be an early indicator for sepsis. HRV is the variation in time intervals between consecutive heartbeats, and it therefore reflects the dynamic, rapidly occurring changes in autonomic regulation caused by the primary systems controlling the heart rate. Multiple features for analyzing these beat-to-beat changes have been constructed and studied in adults. In neonates, on the other hand, HRV has been explored less thoroughly in newborns. A better understanding of autonomic regulation in preterm infants can help to detect deterioration due to sepsis in a more early phase. Therefore, more research is needed to establish reference values for HRV features in preterm infants and variables affecting HRV such as gestational age, postnatal age, gender, breathing rate. In addition, features to detect sepsis in an early stage need to be developed.

Objectives: To investigate in a large population the normal development of Heart Rate Variability parameters and develop machine learning techniques to detect sepsis in an early stage based on vital parameters.

Study design: Observational study, in which a large amount of data was obtained already over a period of more than 2 years.

Student background: Masters student in electrical engineering, biomedical engineering or physics.

Duration: 9-12 months

Student skills: Matlab programming, data analytics, modeling, signal processing and willingness to understand neonatal physiology.

Location: Maxima Medical Center, Veldhoven.

Involved supervisors: Deedee Kommers (postdoc neonatal research), Peter Andriessen (neonatologist); Carola van Pul (clinical physicist); Xi Long (electrical engineering); Ward Cottaar (professor Applied Physics).

References


1.4 Measurement of alarm fatigue

Contact: Carola van Pul  c.v.pul@tue.nl (clinical physicist)

**Background:** The NICU is an intensive care environment in which patients are monitored to keep them within the necessary physiological boundaries. If the patients deteriorate, alarms will attend the caregiver. However, there are so many alarms, many not clinically relevant, that alarm fatigue occurs in clinical practice. Inadequate alarm management is internationally considered the #1 risk at intensive care units. This study will focus on the development of an algorithm to measure alarm relevance and determine the experienced alarm fatigue at NICU.

**Objectives:** to test a setup to measure alarm response using IR beacons and develop an algorithm to determine clinical relevance of alarms and a method to measure the experienced alarm fatigue.

**Study design:** The setup needs to be tested in clinical practice, the algorithm needs to be developed.

**Student background:** Masters student in electrical engineering, biomedical engineering or physics.

**Duration:** 9-12 months

**Student skills:** Matlab programming, data analytics, modeling, signal processing and willingness to understand neonatal physiology.

**Location:** Maxima Medical Center, Veldhoven.

**Involved supervisors:** Deedee Kommers (postdoc neonatal research), Peter Andriessen (neonatologist); Carola van Pul (clinical physicist); Xi Long (electrical engineering); Ward Cottaar (professor Applied Physics). Likely involvement from the Mathematics department.

1.5 Development of a temperature sensor for the Bambi-belt

Contact: Deedee Kommers  deedee.kommers@mmc.nl (researcher, also advisor Bambi Medical)

**Background:** The Bambi Belt Solution is a soft fabric, skin-friendly, wireless monitoring device. It accomplishes the same functions as wired adhesive electrode systems currently implemented in NICUs. A disposable belt functions by being wrapped around baby’s chest. Sensors integrated inside Bambi Belt measure critical data in a nonintrusive way, while a small Sensor Module sends the captured data to our Portable Monitor. However, the temperature sensor still needs to be developed. As a student you participate in the development team and work closely with the Ronald Holst Center.

**Objectives:** to develop a temperature sensor to be used in the belt and test it.

**Student background:** Masters student in electrical engineering, biomedical engineering or physics.

**Duration:** 9-12 months

**Student skills:** Matlab programming, data analytics, modeling, signal processing and willingness to understand neonatal physiology.

**Location:** Maxima Medical Center, Veldhoven / Bambi Medical is located in the Health Innovation Center of MMC.

**Involved supervisors:** Deedee Kommers (postdoc neonatal research), Sidarto Bambang Oetomo (founder of Bambi belt and neonatologist); Carola van Pul (clinical physicist);

http://www.bambi-medical.com/

1.6 Measurement of dose in CT protocols for children – is the current DRL valid?

Contact: Carola van Pul  c.v.pul@tue.nl (clinical physicist)

**Background:** While CT scans have a clear benefit in terms of diagnostics, one should always be aware of the detrimental effects of ionizing radiation. Children are particularly sensitive to these effects, because of their young age and the higher rate of proliferation of their cells. To evaluate whether CT scan doses are as low as reasonably achievable (ALARA), Diagnostic Reference Levels (DRLs) have been published in the Netherlands, for newborns, five-year-old and ten-year-old children. However, the population of pediatric patients receiving CT scans per hospital is so low that benchmarking with respect to DRL is difficult due to the low numbers.

**Study design:** The study will be a multi-center study to determine CT doses and image quality in all centers, evaluate the used protocols and give a suggestion for further optimization.

**Student background:** Masters student in biomedical engineering or physics.

**Duration:** 9-12 months **Student skills:** Matlab programming, modeling, image processing.

**Location:** Maxima Medical Center, Veldhoven.

**Involved supervisors:** Carola van Pul (clinical physicist); Cecile Jeukens (clinical physicist);
2 Projects at University Medical Center Utrecht (UMCU), Utrecht

2.1 Multi-infusion in the neonate.

Contact: Annemoon Timmermans A.M.D.E.Timmerman@umcutrecht.nl (clinical physicist)

Background: Multi-infusion is administering more than one substance directly into the veins of a patient over one access point. In particular in neonates, with their relatively small blood volume, accuracy of infusion is very important for the safe administration of critical medication. Previous research in the joint project by a consortium of UMC Utrecht, and European metrology institutes entitled “Metrology for Drug Delivery (MeDD)” revealed that multi infusion applications, especially of potent, short acting drugs, cause clinically relevant variations in drug delivery. Therefore, standards on how infusion devices should be used contribute to improved stability and accuracy of medication dosage in multi-infusions. This project focuses on improving infusion pump and disposable standards based on improved calibration. A model is developed to predict medication administration.

Objectives: to improve the existing model for medication in multi-infusion systems and check by experiments.

Study Design: a model has been developed in a PhD project and has to be further improved. Validation of the model by experiments using an existing setup should be performed.

Student background: Master student in biomedical engineering or physics.

Duration: 9-12 months

Student skills: Matlab programming, data analytics, modeling, signal processing and willingness to understand physiology.

Location: Utrecht University Medical Center, Utrecht.

Involved supervisors: Annemoon Timmermans (clinical physicist); Carola van Pul (Applied Physics).

3 Projects at Kempenhaeghe, Heeze

3.1 Development and evaluation of Eye Tracking Protocols in clinical neuropsychology

Contact: e.j.e.cottaar@tue.nl

Background: Eyes are a part of the brain. Therefore measurements on eyes/eye movement are seen as a good proxy on the state of the brain. Currently two clinical uses of eye-tracking as investigated in Kemphaeghe are:

- Measuring “attention” in children with attention deficit disorders (ADHD) and other neurological deficiencies (eg. Traumatic brain injury);
- Measuring speed of information processing in epilepsy and possible side effects of anti-epileptic drugs (this can be done in combination with other modalities (like EEG);

Present status: New technology (hardware) has been obtained by Kempenhaeghe which allows for more accurate measurements with a better time resolution of eye movements (and other aspects like pupil size) than has been available so far. First protocols have been developed. Currently evaluation of eye tracking data is done based on visual inspection by the clinician/researcher.

Objectives: to develop algorithms which allow for a fast, accurate and automated analysis of the measurements.

- Implement algorithms for the available hardware based on known mechanisms and clinicians/researchers’ insights
- Using statistical tools/machine learning mechanisms to find new relevant parameters in the available data. Of course, in combination with psychological insights.

Student background: student in biomedical engineering, electrical engineering, or physics.

Duration: 9-12 months

Student skills: Matlab programming, data analytics, modeling, signal processing and willingness to understand physiology. Good communication skills (Testing and development of algorithms will also involve execution of experiments with patients (including children).

Location: Kempenhaeghe, Heeze

4 Projects at Jeroen Bosch Ziekenhuis, ’s Hertogenbosch

4.1 Cardiac imaging in Nuclear Medicine

Contact: Dr. ir. C.H.L. (Chris) Peters (c.peters@jbz.nl)

Het Jeroen Bosch Ziekenhuis loopt voorop in Nederland op het gebied van nucleaire cardiologische diagnostiek. Voor het verrichten van myocard perfusie onderzoek heeft het ziekenhuis zelf een generator ontwikkeld waarmee radioactief rubidium geproduceerd kan worden. Met deze innovatie is een grote stap gezet op het gebied van patiëntvriendelijkheid doordat de stralingsbelasting van het onderzoek met een factor 3 gereduceerd wordt en de verblijftijd van de patiënt in het ziekenhuis verkort wordt van 5 uur tot slechts 1 uur. Om het potentieel van de innovatie optimaal te benutten voor betere diagnostiek, dient echter nog een aantal stappen gezet te worden. Dit project richt zich op het beter benutten van de extra informatie die myocard perfusie onderzoek met rubidium verstrekt. In het bijzonder zal de absolute kwantificering van flow in het myocard gevalideerd worden met behulp van een in-vitro kloppend hart dat voorzien is van Doppler flowsensoren om de coronaire arteriën. Door in meerdere geïnstrumenteerde harten stenoses aan te brengen die verschillen in locatie en omvang, wordt een representatieve doorsnede van patiëntenpopulatie gesimuleerd. Op deze wijze worden unieke resultaten verkregen die in grote mate kunnen bijdragen aan de acceptatie van absolute kwantitatieve flow en/of flow reserve binnen de diagnostiek van coronaire hartziekten.

Doel: Het huidige voorstel betreft het uitvoeren van een pilot in-vitro experiment om de haalbaarheid van de experimentele opzet aan te tonen. Deze fase kan door een afstudeerder worden uitgevoerd.

Student background: Masters student in biomedical engineering or physics.

Availability: 9-12 months

Student skills: Matlab programming, data analytics, modeling, signal processing

Location: Jeroen Bosch Ziekenhuis, Den Bosch.

Involved supervisors: Chris Peters (clinical physicist)

5 Projects at Catharina Ziekenhuis Eindhoven

5.1 Obtaining the actual delivered dose for image-guided online adaptive radiotherapy

Contact: danny.schuring@catharinaziekenhuis.nl (clinical physicist)

Background: The radiotherapy treatment nowadays is mainly based on a treatment plan derived from a single CT “snapshot” of the patient anatomy, and then performing daily treatment without accounting for changes in this anatomy. For organs with large deformations, such as the bladder, this can result in a mistreatment of the tumor or complications due to the irradiation of healthy tissue. By estimating the shape variations at the start of treatment (e.g. by using an empty and full bladder scan), creating a library of plans accounting for these variations, and selecting the appropriate plan based on daily pre-treatment imaging, a more effective treatment can be given. With the introduction of online MR-guided radiotherapy, further possibilities are opening up for applying this online adaptive approach. Adding the daily delivered doses to obtain the total dose given to the patient is not a straightforward problem. Using deformable image registration, displacements of each voxel in an organ can be determined, and an accumulated dose can be calculated.

Objectives: To implement improvements to our clinical online adaptive radiotherapy treatment (specifically for bladder cancer), and develop and validate a method for calculating the total delivered dose to a patient from the daily selected plans.

Study design:

• Develop a method to create synthetic CTs of intermediate organ shapes based on empty and full bladder scans, and validate these using daily cone-beam CT images.
• Use deformable image registration and dose accumulation to determine the actual delivered dose for patients treated clinically with this online adaptive procedure.
• Validate the dose accumulation by looking at registration uncertainties and their effect on the accumulated dose.
• Create an efficient workflow for calculating these dose accumulations using Python scripting.
• Evaluate the gains from these adaptive treatments, and explore possibilities for further improvement.

Student background: Masters student in biomedical engineering or physics.
Availability: 9-12 months
Student skills: Matlab programming, data analytics, modeling, signal processing
Location: Radiation Oncology Department, Catharina Hospital Eindhoven.
Involved supervisors: Danny Schuring (clinical physicist); Coen Hurkmans (clinical physicist)

5.2 A prediction model of the effect of delineation uncertainties on dose

Contact: Coen Hurkmans coen.hurkmans@catharinaziekenhuis.nl

Background: Patients with cancer can be treated in various ways, usually with a combination of surgery, chemotherapy, immunotherapy and radiotherapy. With radiotherapy, a high radiation dose is given to the tumor while sparing the surrounding tissue as much as possible. These treatment plans are based on, usually manual, delineations of the tumor and organs at risk. Variations in delineations will lead to variations in the dose delivered to the actual tumor and organs at risk. This will lead to a decrease in treatment efficacy.

Objectives: To determine the delineation variation in and its impact on the planned dose for patients treated in the European Organization of Research and Treatment of Cancer 1709 Glioblastoma clinical trial. Furthermore, to develop new methods/tools to incorporate delineation variations in the evaluation of the appropriateness of planned dose distributions.

Study design:
• Use the benchmark plan data available within the EORTC 1709 trial to quantify delineation variations.
• Quantify the variation in dose resulting from these variations.
• Develop and test new methods to predict the influence of delineation variations on dose.
• Based on this new prediction model, suggest guidelines for QA in future clinical trials.
• Compare the results with similar results as reported in the literature

Student background: Masters student in biomedical engineering or physics.
Availability: 9-12 months
Student skills: Matlab programming, data analytics, modeling, signal processing
Location: Radiation Oncology Department, Catharina Hospital Eindhoven.
Involved supervisors: Coen Hurkmans (clinical physicist)

5.3 Dosimetric benefit of on-line set-up corrections for radiotherapy of lung cancer patients

Contact: Coen Hurkmans coen.hurkmans@catharinaziekenhuis.nl

Background: Patients with cancer can be treated in various ways, usually with a combination of surgery, chemotherapy, immunotherapy and radiotherapy. With radiotherapy, a high radiation dose is given to the tumor while sparing the surrounding tissue as much as possible. For lung cancer patients, the set-up of the patient at the treatment unit needs to be as close as possible to the planned position. Until a few years ago not all set-up errors were corrected. Over the last 3 years, all set-up errors are corrected using 3D cone-beam CT (CBCT) imaging at the treatment unit.

Objective: To determine if the introduction of on-line CBCT guided set-up corrections for lung cancer patients improves overall survival. A second objective is to determine how the relationship between tumor position and organs at risk changes over a course of radiotherapy and how this translates into dose variations

Study design:
• Develop and implement methods to (semi-)automatically determine the shifts of a tumor in relation to organs at risk in CBCT images.
• Determine the actual accumulated dose over a course of radiotherapy using CT and CBCT data and deformable registration.
• Quantify the set-up shifts and correlate these with dose variations.
• Compare the results with similar results as reported in the literature.

Student background: Masters student in biomedical engineering or physics.
Availability: 9-12 months
Student skills: Matlab programming, data analytics, modeling, signal processing
5.4 Optimization of breast cancer patient treatment plans

contact: Coen Hurkmans coen.hurkmans@catharinaziekenhuis.nl

Background: Patients with cancer can be treated in various ways, usually with a combination of surgery, chemotherapy, immunotherapy and radiotherapy. With radiotherapy, a high radiation dose is given to the tumor while sparing the surrounding tissue as much as possible. For breast cancer patients, the dose given to the breast needs to be balanced against the dose given to the lungs and the heart. Based on international guidelines, the number of irradiation fractions and the nominal dose per fraction is harmonized. However, in current practice on use is made of previously generated treatment plans. Also, the optimization does not take the position of the primary tumor into account or patient related cardiac morbidity risk factors.

Objective: To automatically determine the optimal individual breast cancer radiotherapy treatment plan based on the position of the primary tumor and the individual cardiac morbidity risk factors.

Study design:
• Develop and implement methods to optimize treatment plans based on the location of the primary tumor and the individual cardiac morbidity risk factors. This might include some scripting in python.
• Quantify the reduction in cardiac toxicity resulting from this individualized optimization.
• Develop and validate the generation of new plans based on previously generated plans using a large clinical database of plans and artificial intelligence solutions (based on software tools available in the research version of our planning system)
• Compare the results with similar results as reported in the literature

Student background: Masters student in biomedical engineering or physics.
Availability: 9-12 months

Student skills: Matlab programming, data analytics, modeling, signal processing

Location: Radiation Oncology Department, Catharina Hospital Eindhoven.
Involved supervisors: Coen Hurkmans (clinical physicist)

6 Projects at Maastricht University Medical Center (MUMC), Maastricht

There are usually also projects possible in MUMC. Currently no description exist but you can contact Carola (c.v.pul@tue.nl) or Cecile Jeukens directly (cecile.jeukens@mumc.nl) for possibilities.