TTÜ TEHNOMEEDIKUMI INSTITUUDI TEADUS- JA ARENDUSTEGEVUSE AASTAARUANNE 2011

1. Struktuur

Direktor Kalju Meigas

- **Biomeditsiinitehnika instituut, Department of Biomedical Engineering,** Ivo Fridolin
  - Biomeditsiinitehnika õppetool, Chair of Biomedical Engineering, Kalju Meigas
  - Meditsiinifüüsika õppetool, Chair of Medical Physics, Ivo Fridolin
- **Kardioloogiakeskus, Centre of Cardiology,** Jüri Kaik
  - Elektrofüsioloogia õppetool, Chair of Electrophysiology, Jüri Kaik
- **Kliinilise meditsiini instituut, Department of Clinical Medicine,** Ruth Sepper
  - Kliinilise meditsiini õppetool, Chair of Clinical Medicine, Ruth Sepper
  - Tervishoiutehnoloogia õppetool, Chair of Health Care Technology, kt. Kaiu Prikk

2. Teadus- ja arendustegevuse (edaspidi T&A) iseloomustus

Research and development activities of Technomedicum (TM) cover medicine, technology and biomedicine, degree studies related to medicine, biomedicine and technology, relevant continuing education courses as well as teaching of medical disciplines organized by other TUT academic units on the master and doctoral level. In addition to TUT academic and research staff, doctor-teachers and doctor-researchers from several hospitals participate in TM academic and research activities.

The structure of TM includes Department of Biomedical Engineering, Department of Clinical Medicine and Centre of Cardiology.

2.1.1. teadustöö kirjeldus *(inglise keeles*);

- **NMR group**: Research concentrated on NMR engineering, as a basis on novel experiments and increased analytical capacity. Simultaneously, associated methods were numerically analyzed and optimized.

2.1.2. aruandeaastal saadud tähtsamad teadustulemused *(inglise keeles*)

- We were able do increase speed of magic angle spinning from 80 to 90 kHz. A new stepper motor actuated angle switching mechanism was designed, constructed and tested. Metabolites in a first batch of body liquid samples were identified and quatified.

2.2. Uurimisgrupi kuni 5 olulisemat publikatsiooni läinud aastal

- Nielsen Ulla Gro; Heinmaa Ivo; Samoson Ago; et al. “Insight into the Local Magnetic Environments and Deuteron Mobility in Jarosite (AFe(3)(SO(4))(2)(OD,OD(2))(6), A = K, Na, D(3)O) and Hydronium Alunite ((D(3)O)Al(3)(SO(4))(2)(OD)(6)), from Variable-Temperature (2)H MAS NMR Spectroscopy”, Chemistry of Materials, Vol. 23 Issue 13, pp. 3176-3187. 2011
- Howes A. P.; Vedishcheva N. M.; Samoson A.; et al. “Boron environments in Pyrex (R) glass-a high resolution, Double-Rotation NMR and thermodynamic modelling study”, Physical Chemistry Chemical Physics. Vol. 13 Issue 25, pp. 11919-11928, 2011
- Hou Guangjin; Yan Si; Sun Shangjin; Samoson Ago; et al. “Spin Diffusion Driven by R-Symmetry Sequences: Applications to Homonuclear Correlation Spectroscopy in MAS NMR of Biological and Organic Solids”, Journal of the American Chemical Society. Vol. 133, Issue 11, pp. 3943-3953, 2011

- Becker-Baldus Johanna; Kemp Thomas F.; Past Jaan; Samoson Ago, et al. "Longer-range distances by spinning-angle-encoding solid-state NMR spectroscopy", Physical Chemistry Chemical Physics, Vol. 13, Issue 10, pp. 4514-4518, 2011

2.3 Loetelu struktuuriüksuse töötajate rahvusvahelistest tunnustustustest.
Ago Samoson - Invited lectures at Indian and Bulgarian National NMR conferences, also at a conference of International Peptide Society

2.4 Loetelu struktuuriüksuse töötajatest, kes on välisakadeemiate või muude oluliste T&A-ga seotud välisorganisatsioonide liikmed.

A.Samoson: ISMAR Fellow, National representative at AMPERE and ESF EMAR.

2.5 Aruandeaasta tähtsamad T&A finantseerimise allikad.

FP7, TTÜ baasfinantseerimine, DoRa, Mobilitas

2.6. Soovi korral lisada aruandeaastal saadud T&A-ga seotud tunnustusi (va punktis 2.3 toodud tunnustused), ülevaate teaduskorralduslikust tegevusest, teadlasmobiilsusest ning anda hinnang oma teadustulemustele.

Mitme regionaalse *workshopp*'i organiseerimine
12.-13.03.2011 D/RNA NMR
13.05.2011 Mathematics, Metabolomics and NMR;
7.12.2011 Quantitative (metabonomics in) medicine.

Biomeditsiinitehnika instituudi (**Department of Biomedical Engineering**) T&A iseloomustus
2.1 teadustöö kirjeldus *(inglise keeles*);

- **Biofluid optics:** The aim of the BFO team was to develop an optical technology for monitoring of uremic toxins related to malnutrition-inflammation complex syndrome (MIA) on the ESRD patients and to CVD risk in general. Estonian-Swedish multicenter analysis revealed that concentration of the small water-soluble uremic retention solute creatinine, a marker for malnutrition estimation, can be successfully estimated in the spent dialysate in larger patient populations. Development of a novel method for determining middle and protein bound uremic toxins, markers for MIA and CVD risk, in the spent dialysate utilizing fluorescence was continued. Clinical experiments were carried out in North Estonian Medical Centre during which on-line spectrophotometrical and fluorimetrical monitoring was performed in parallel first time in the world. The project group participates in the Estonian Centre of Excellence CEBE.
- **Diagnostics of cardiovascular diseases:** Atherosclerosis is the main cause for deaths in Europe. Early preventive actions are essentially important as Estonia have the highest mortality level for heart-vascular diseases in Europe. Improvement of non-invasive methods for diagnostics of atherosclerosis in very early stage is extremely important. The aim of our research is to develop a new methodology to determine dynamic compliance of arteries and consider usefulness in early diagnostics of atherosclerosis on the basis of optical methods worked out by our group for arterial blood pressure monitoring. The hypothesis is that simultaneous and quick registration of mechanical movements of arteries walls, pulse wave velocity and shape, and dynamics of blood pressure creates a system of parameters for estimation of dynamic compliance of arteries and to get early diagnoses of atherosclerosis. Expected results: Complex optical method for early diagnose of atherosclerosis will be developed. Different physiological parameters and technical solutions (e.g. mechanical movements of arteries, pulse wave shape, pulse wave velocity and local blood pressure) will be investigated**.**

- **Brain research:** The research activity was aimed to development of quantitative measures and algorithms for estimation of characteristic changes in the EEG related to the state of the brain, mental disorders and effect of external physical stressor on the brain. For this purpose, the linear and nonlinear methods for 1) modelling of the processes in the brain (nonlinear parametric excitation) and 2) EEG signal analysis (integration of differences, fractal dimension) were applied.

  1) The model of parametric excitation based on polarization of water molecules was proposed and experimental results compared to the model. The experiments were carried out on 28 human volunteers. The 450 MHz microwave radiation modulated at 7, 14, 21, 40 and 70 Hz frequencies was applied at the field power density 0.16 mW/cm**2**. The resting EEG was recorded in 8 channels and EEG power at selected frequencies was analyzed. A relative change in the EEG power during 10 cycles with and without radiation was used as a quantitative measure. Microwave radiation caused an increase in the average EEG power in all selected EEG frequency bands. Increase in the EEG power was statistically significant only at the EEG frequency ***f0*** to modulation frequency *F* ratios ***f0*** */F* □ 0.25, 0.5 and 0.75. Results of the experimental study are in accordance with the proposed model of parametric excitation of the brain neural oscillations and demonstrate that modulated microwave radiation causes excitation of the brain EEG rhythms at the frequencies predicted by the non-linear model.

  2) Higuchi's fractal dimension (FD) as a measure was applied to evaluate the effect of external periodic stressor on electrical oscillations in the brain. Modulated microwave radiation was used as a weak periodic stressor with strongly inhomogeneous distribution inside the brain. Experiments were performed on a group of 14 volunteers. Ten cycles (1 min on, 1 min off) of 450-MHz microwave radiation modulated at 40 Hz were applied. Higuchi's FD was calculated in eight symmetric electroencephalographic (EEG) channels located in frontal, temporal, parietal, and occipital areas. FD values averaged over a group detected a small (1–2%) but statistically significant increase with exposure in all EEG channels. FD increased for 12, decreased for one, and was constant for one subject. FD showed the most remarkable effect in temporal and parietal regions of the left hemisphere where the microwave field was maximal. Changes of FD in these regions of the right hemisphere were much higher than expected in accordance with the field distribution. Correlation of FD between different EEG channels was high and retained its value in exposed conditions.

1.1.1 aruandeaastal saadud tähtsamad teadustulemused *(inglise keeles).*

- **Biofluid optics:** One 1.2 and 2 international conference 3.1 publications, one 3.2 book chapter and three 5.2 conference abstracts were published. 3 international patent application were filed (P201100002, PCT/EE2011/000005, PCT/EE2011/000008). 2 CC publications were submitted (1st positive review achieved).
- **Diagnostics of cardiovascular diseases:** Developed a new methodology for early diagnosis of atherosclerosis based on optical non-invasive determination of dynamic compliance of arteries. Novelty is within a dramatic improvement of time in simultaneous and quick optical registration of mechanical movements of arteries walls, pulse wave velocity and shape, and dynamics of blood pressure creates a system of parameters for estimation of dynamic compliance of arteries and to get early diagnoses of atherosclerosis.
  Cooperation: North Estonia Medical Centre, Tallinn (Estonia), Optoelectronics and Measurement Techniques Laboratory, University of Oulu, Centre for Integrated Electronic Systems and Biomedical Engineering (CEBE). **Signal processing methods.** The number of physiological signals and reference parameters (pulse waves from different locations of the body, peripheral pressure pulse wave, electrocardiographic signal, phonocardiography waves, augmentation indices and pulse wave velocity in aorta) has been measured from volunteers and atherosclerotic patients (diabetes mellitus). The novelty is in the concept for the development of

the new optical method and its evaluation. The new signal processing methods have been developed and are currently under development in cooperation between TM Cardiology Team and ELIN Signal Processing Team in order to extract the physiological parameters for the early diagnose of arthrosclerosis from the recorded pulse wave shape.
Cooperation: North Estonia Medical Centre, Tallinn (Estonia), Optoelectronics and Measurement Techniques Laboratory, University of Oulu, Department of Biomedical Engineering, Linköping University, Centre for Integrated Electronic Systems and Biomedical Engineering (CEBE).

- **Brain research:** 1) Physical model of nonlinear parametric excitation of the brain by modulated microwave radiation was developed and proved by experimental data. The proposed model is solution for decades-long world-wide discussion on non-thermal microwave effects. Our results at first time provide both, an experimental evidence for modulated microwaves effects on EEG and a theoretical framework that predicts the results.
  2) Detection of microwave effects at the level of radiation much lower than the existing health protection limits is especially important in light of the recent document of the Council of Europe (Resolution 1815 from 27 May 2011 The potential dangers of electromagnetic fields and their effect on the environment).
  3) Distribution of alterations in the EEG fractal dimension (FD) in different brain regions showed that related to microwave exposure alterations were much stronger than expected according to the field distribution in the brain. Spreading of disturbance between different brain areas is supposed to be crucial for the effect of exposure on the electrical oscillations in the brain. This finding confirms nonlinear behaviour of the brain and strong correlation between brain areas.

2.2 Uurimisgrupi kuni 5 olulisemat publikatsiooni läinud aastal.

Biofluid optics:

- Jana Holmar, Jürgen Arund, Fredrik Uhlin, Risto Tanner, Ivo Fridolin, "Beta2-microglobulin Measurements in the Spent Dialysate Using Fluorescence Spectra", 5th European Conference of the International Federation for Medical and Biological Engineering,14-18 September, 2011, Budapest, Hungary, vol. 37, pp. 1035 - 1038, 2011.
- Tomson, R.; Uhlin, F.; Holmar, J.; Lauri, K.; Luman, M.; Fridolin, I. (2011). Development of a method for optical monitoring of creatinine in the spent dialysate. Estonian Journal of Engineering, 17(2), 140 - 150.
- Lauri, K.; Arund, J.; Holmar, J.; Tanner, R.; Luman, M.; Fridolin, I. (2011). Optical Dialysis Adequacy Monitoring: Small Uremic Toxins and Contribution to UV-Absorbance Studied by HPLC. Angelo Carpi, Carlo Donadio and Gianfranco Tramonti (Toim.). Progress in Hemodialysis - From Emergent Biotechnology to Clinical Practice (143 - 160).InTech - Open Access Publisher

Diagnostics of cardiovascular diseases:

- HYPEST study: profile of hypertensive patients in Estonia, Org E, Veldre G, Viigimaa M, Juhanson P, Putku M, Rosenberg M, Tomberg K, Uuetoa T, Laan M., BMC Cardiovasc Disord. 2011 Aug 31;11:55.
- Hypertension and sexual dysfunction: time to act, Viigimaa M, Doumas M, Vlachopoulos C, Anyfanti P, Wolf J, Narkiewicz K, Mancia GJ Hypertens. 2011 Feb;29(2):403-7.
- Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk, International Consortium for Blood Pressure Genome-Wide Association Studies incl. Viigimaa M. Nature. 2011 Sep 11;478(7367):103-9.
- Cardiovascular disease risk factors in homeless people, Kaldmäe M, Zilmer M, Viigimaa M, Zemtsovskaja G, Tomberg K, Kaart T, Annuk M., Ups J Med Sci. 2011 Aug;116(3):200-7. Epub 2011 Jun 22.

- Novel polymorphic AluYb8 insertion in the WNK1 gene is associated with blood pressure variation in Europeans, Putku M, Kepp K, Org E, Sõber S, Comas D, Viigimaa M, Veldre G, Juhanson P, Hallast P, Tõnisson N; HYPertension in ESTonia (HYPEST), Shaw-Hawkins S, Caulfield MJ; BRItish Genetics of HyperTension (BRIGHT), Khusnutdinova E, Kožich V, Munroe PB, Laan M., Hum Mutat. 2011 Jul; 32(7):806-14. doi: 10.1002/humu.21508. Epub 2011 May 10.

Brain research:

- Hiie Hinrikus, Maie Bachmann, and Jaanus Lass. Parametric mechanism of excitation of the electroencephalographic rhythms by modulated microwave radiation. International Journal of Radiation Biology 2011, 87:1077-1085
- Hinrikus H, Bachmann M, Karai D, Klonowski W, Lass J, Stepien P, Stepien R, Tuulik V. Higuchi's fractal dimension for analysis of the effect of external periodic stressor on electrical oscillations in the brain. Medical & Biological Engineering & Computing 2011, 49(5):585-591.

2.3 Loetelu struktuuriüksuse töötajate rahvusvahelistest tunnustustustest.

- **The first award to Kristjan Pilt in the poster category at IFMBE Young Investigator Competition at 15th NBC on Biomedical Engineering & Medical Physics for the publication** K. Pilt, K. Meigas, M. Viigimaa and K. Temitski, "Possibility to use Finapres signal for augmentation index estimation", NBC 2011, IFMBE Proceedings, 2011, Volume 34, pp. 25-28.
- **A finalist award to Jana Holmar at IFMBE Young Investigator Competition at 5th European Conference of the International Federation for Medical and Biological Engineering for the publication and the oral presentation;** Jana Holmar, Jürgen Arund, Fredrik Uhlin, Risto Tanner, Ivo Fridolin, "Beta2-microglobulin Measurements in the Spent Dialysate Using Fluorescence Spectra", 5th European Conference of the International Federation for Medical and Biological Engineering,14-18 September, 2011, Budapest, Hungary, vol. 37, pp. 1035 - 1038, 2011.

2.4 Loetelu struktuuriüksuse töötajatest, kes on välisakadeemiate või muude oluliste T&A-ga seotud välisorganisatsioonide liikmed.

Hiie Hinrikus - International Academy for Medical and Biological Engineering (IAMBE), Fellow

Margus Viigimaa - Euroopa Hüpertensiooni Ühingu juhatuse liige ja töögrupi „Hüpertensioon ja seksuaalne düsfunktsioon“ juhataja ning rahvusvaheliste teadusajakirjade "Blood pressure", “Journal of Hypertension” ja “Seminars in Cardiology” toimetuste liige;

Kalju Meigas - rahvusvahelise ühingu IFMBE meditsiinitehnoloogia divisjoni juhatuse liige ja rahvusvaheliste teadusajakirjade “Measurement Science Review” ja “Bioelectromagnetism” toimetuste liige, samuti rahvusvahelise doktorikooli “International Graduate School in Biomedical Engineering and Medical Physics” juhatuse (management board) liige.

2.5 Aruandeaasta tähtsamad T&A finantseerimise allikad.

- SF0140027s07, Biosignaalide interpreteerimine meditsiinitehnikas, sihtfinantseeritav teema
- Integreeritud elektroonikasüsteemide ja biomeditsiinitehnika tippkeskus CEBE – Eesti tippkeksus
- Uudne optiline meetod ureemiliste toksiinide - alatoitumuse ja kroonilise põletiku ning SVH riski potentsiaalsete markerite, monitooringuks – ETF grant

2.6 Soovi korral lisada aruandeaastal saadud T&A-ga seotud tunnustusi (va punktis 2.3 toodud tunnustused), ülevaate teaduskorralduslikust tegevusest, teadlasmobiilsusest ning anda hinnang oma teadustulemustele.

Kardioloogiakeskuse (**Centre of Cardiology**) T&A iseloomustus

2.1.1 aruandeaastal teadustöö kirjeldus *(inglise keeles*);

In 2011 the sub-study of targeted financed project SF0140027s07 "Interpretation of Bioelectrical Signals" was carried out in the Centre of Cardiology. . This project is the continuation of the research carried out in Estonian Institute of Cardiology and Centre of Cardiology, Technomedicum of Tallinn University of Technology, during past 13 years - evaluating the level of myocardial electrical instability (MEI) by assessment of non-invasive markers of ventricular repolarization (VR) prolongation and inhomogeneity.

During the last decade, much attention has been focused on the investigation of VR and numerous new approaches for analysis of QT interval spatial and temporal variability have been developed and reported to possess considerable prognostic value for predicting sudden cardiac death (SD). Newly emerging gender differences in the pathophysiology of VR imply the need for evaluation of more specific and sensitive methods of VR assessment.

The aim of our team's study was to investigate the correlation between non-invasive markers of prolonged and inhomogeneic VR, which can be used for improvement of SD risk stratification and prediction of antiarrhythmic drug treatment efficacy/arrhythmogenic effect in patients with various heart diseases. The hypothesis presumes, that a combination of different indicators will improve SD risk stratification and prediction of antiarrhythmic drug treatment efficacy/arrhythmogenic effect.

During 2011 new approach for predicting of SCD were developed based on non-invasive VR parameters evaluation using physiological, biochemical and radioimmunological investigations and assessing QT interval parameters characterizing VR during ECG 24-hour recording at exercise test and transesophageal electrophysiologic study. New algorithms for ECG QT interval variability and QT interval rate-adaptation evaluation, which (1) essentially correlate with generally recognized markers of elevated myocardial electrical instability, such as high-grade ventricular ectopy, low ejection fraction, decreased heart rate variability, etc , (2) do not depend on (or do so to a very limited extent) changes of structure of left ventricle (myocardial infarction, heart failure, left ventricular hypertrophy), and (3) can be easily adapted for Holter monitor or ECG device are used in sleep research in Estonian sleep medicine centers.

1.1.1 aruandeaastal saadud tähtsamad teadustulemused (inglise keeles)

We applird different novel QT/RR regression models and heart rate correction formulas to clinical 24-hour ECG recordings, providing QTc interval values that are independent of corresponding RR interval values, that were developed in healthy patients using short isolated HM strips , and to evaluate the discriminating significance of this approach for patients with different MEI levels assessed by maximal Lown grade of spontaneous ventricular arrhythmias during recording, which has unequivocally demonstrated its independent prognostic value

1. The algorithm developed during the study enables application of novel QT interval correction and QT/RR ratio determination models in routinely registered ECG 24-hour recordings in patients with various heart diseases and without overt heart disease.
2. Significant intra- and intersubject variability of QTc and QT/RR ratio was recorded in patients with different levels of myocardial electrical instability, so in order to obtain "ideal" correction (zero correlation), individual parameter alpha values should be applied to every single person

The QTc deviation values obtained by linear correction model, differed significantly in patients with various MEI levels, so, if it is further validated, it could be used as a method for arrhythmia risk stratification

During the year our team established and deepened international and national cooperation in the field of developing new algorithms for ECG QT interval variability and QT interval rate-adaptation evaluation, feasible for noninvasive detection of high sudden death risk in cardiac patients with Saint Joseph College (West Hartford, CT. USA) and Mae Pindmaa Sleep Medicine Centre (Estonia), as well in the field cardiac aspects of sleep medicine with Mae Pindmaa Sleep Medicine Centre (Estonia), University of Turku, Department of Physiology, Sleep Research Unit (Turku, Finland), Sahlgrenska Academy, Dept of Internal Medicine; Institute of Medicine (Gothenburg, Sweden) Almazov Federal Research Centre for Cardiology, Vasology and Endocrinology (St. Petersburg; Russia). Common European platform for transferring and processing wireless biological signals is developed in cooperation with Unesta OY (Finland) and ITMO University (St. Petersburg; Russia). 1 CC publications was submitted (and positive review achieved) Shipilova, T.; Pshenichnikov, I.,; Riipulk, J.; Karai, D.; Kaik, J. Heart rate daily profile in assessment of subclinical organ damage in patients with arterial hypertension.

2.2 Uurimisgrupi kuni 5 olulisemat publikatsiooni läinud aastal.

- Pshenichnikov, I.; Shipilova, T.; Karai, D.; Riipulk, J., Veski, K.; Pilt, K.; Kaik, J. (2011). Association between ventricular repolarization and main cardiovascular risk factors. Scandinavian Cardiovascular Journal, 45 (1), 33 – 40.
- Shipilova, T.; Abina, J.; Pshenitchnikov, I.; Karai, D.; Riipulk, J.; Kaik, J. (2011) Main cardiovascular risk factors and hypertension in a subgroup of women population In Tallinn during 10 years of follow-up. Journal of Hypertension: 21 annual meeting of ESH., 2011, e298 – e298

2.3 Loetelu struktuuriüksuse töötajate rahvusvahelistest tunnustustustest.

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2.4 Loetelu struktuuriüksuse töötajatest, kes on välisakadeemiate või muude oluliste T&A-ga seotud välisorganisatsioonide liikmed.

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2.5 Aruandeaasta tähtsamad T&A finantseerimise allikad.

- Põhiteema nr. SF0140027s07 „Biosignaalide interpreteerimine meditsiinitehnikas „
- Baasfinanseerimisteema nr. BF 151 „TTÜ Tehnomeedikumi kardioloogiakeskus“

2.6 Soovi korral lisada aruandeaastal saadud T&A-ga seotud tunnustusi (va punktis 2.3 toodud tunnustused), ülevaate teaduskorralduslikust tegevusest, teadlasmobiilsusest ning anda hinnang oma teadustulemustele.

- TM Kardioloogiakeskuse arengukavas 2011.aastaks ettenähtud ülesanded täideti.
- Keskus osales aktiivselt tehnomeedikumi alusuuringus „ Bioelektriliste signaalide interpreteerimine meditsiinitehnikas.“ Nr.0140027s07
- Keskuse teadurid (2,25 koormusega akadeemilist töötajat) valmistasid ette ja osalesid alusuuringu teemakohaste artiklite publitseerimises.
- Jätkus tegevus Integreeritud Elekroonikasüsteemide ja Biomeditsiinitehnika Tippkeskuses CEBE.
- Keskuse töös osaleb 2 doktoranti.
- Keskus töötab jätkuvalt väga raskes finantsolukorras.
- 2012.a. on kardioloogiakeskuse ülesandeks jätkata aktiivset teadus-ja arendustegevust. Valmistada ette ja publitseerida artikleid täidetava alusuuringu temaatikast. Leida võimalusi uute projektide käivitamiseks.

Kliinilise meditsiini instituudi (**Department of Clinical Medicine)** T&A iseloomustus

Kliinilise meditsiini instituut lisab kompetentsi TTÜ eelisarendatavate valdkondade (keemia- ja biotehnoloogia, biomeditsiini) arendusse, sobindudes “Keemia, biotehnoloogia ja biomeditsiini valdkonna teadus- ja arendustegevuse programmi aastateks 2005-2015” (TTÜ, 2005).

Meie üheks eesmärgiks on sulandada arstiteadust Tehnikaülikooli loodusteadustega ja tehnoloogiaga. Oleme suutnud kaasata akadeemilisse töösse kvalifitseeritud arstid ja tõstnud nende huvi teadustegevuse vastu: arstid on asunud õppima doktorantuuris ning oleme kaasanud lisaks ülikoolis juba töötavatele teadlastele uusi teaduskraadiga arste (Dr. Katrin Gross-Paju, MD, PhD, Dr. Anu Kasmel MD, MSc, dots. Andres Soosaar, MD, PhD, Dr. Peeter Ross, PhD, Dr. Madis Tiik).
Kliinilise meditsiini instituudi teadus- ja arendustegevuse valdkonnad on:

- Astma ja kroonilise obstruktiivse kopsuhaiguse tekke, arengu ja varase diagnostika uurimise põhjused (*Investigations on causes and development and early diagnostics of asthma and chronic obstructive lung disease).* Teadussuuna juht prof. Ruth Sepper, kaastöötajad van. teadur Kaiu Prikk, prof. Thomas Fehniger, doktorandid Berit Pilden, Sirje Marran ja Ave Nagelmann.
- E-tervise teadussuund (*E-health),* mida juhib rahvusvaheline teadlaskond, kuhu kuuluvad Tallinna ja Helsingi Tehnikaülikooli dotsent Hanna Pohjonen, teadur Kalev Karu, projektijuht Madis Tiik, MD, ja projekti koordinaator Peeter Ross, PhD.

2.1.1 teadustöö kirjeldus *(inglise keeles*);

- Investigations on causes and development and early diagnostics of asthma and chronic obstructive lung disease
- E-health, development of projects „*eMedic – Developing New Practices for Teleconsultation and Diabetes", "PrimCare IT - Counteracting brain drain and professional isolation of health professionals in remote primary health care through tele-consultation and tele-mentoring to strengthen social conditions in remote BSR"*

2.1.2. aruandeaastal saadud tähtsamad teadustulemused *(inglise keeles).*

- We demonstrated that lung function deviation and lung structural changes are present in chronic smokers before the clinical signs of airway obstruction reveal and these changes are associated with early onset of chronic obstructive pulmonary disease (COPD).
- We demonstrated as a proof-of-principle the tissue uptake of an inhaled drug in the *in vivo* lung by use of matrix-assisted laser desorption inozation mass spectrometry imaging analysis.

2.2 Uurimisgrupi kuni 5 olulisemat publikatsiooni läinud aastal.

- Fehniger, T.E.; Végvári, A.; Rezeli, M.; Prikk, K; Ross, P.; Dahlbäck, M.; Edula, G.; Sepper, R.; Marko-Varga, G. (2011). Direct Demonstration of Tissue Uptake of an Inhaled Drug: Proof-of-Principle Study Using Matrix-Assisted Laser Desorption Ionization Mass Spectrometry Imaging. Analytical Chemistry, 83(21), 8329 - 8336.
- Sepper R, Ross P, Tiik M. (2011).Nationwide Health Data Management System: a novel approach for integrating biomarker measurements with comprehensive health records in large populations studies. J Proteome Res. 10:97-100.
- Marko-Varga, G.; Fehniger, T. E.; Rezeli, M.; Döme, B., Laurell, T.; Végvári, A. (2011). Drug localization in different lung cancer phenotypes by MALDI mass spectrometry imaging. Journal of Proteomics, 74(7), 982 - 992
- Nagelmann A, Tonnov Ä, Laks T, Sepper R, Prikk K. (2011). Lung dysfunction of chronic smokers with no signs of COPD. COPD, 8:189-95.
- Marran, S, Vanakesa, T, Sepper, R. (2011). Changing diagnostic strategies of mediastinal and hilar lymphadenopathies: EBUS-TBNA diagnosing benign lesions. ScienceMed, 1: 41 - 46.

2.3 Loetelu struktuuriüksuse töötajate rahvusvahelistest tunnustustustest.

2011. aastal struktuuriüksuse töötajaid rahvusvaheliselt ei tunnustatud.

2.4 Loetelu struktuuriüksuse töötajatest, kes on välisakadeemiate või muude oluliste T&A-ga seotud välisorganisatsioonide liikmed.

Ruth Sepper	-	FP7 Programm Tervis programmikomitee, ekspert Marie Curie Individual fellowships, Panel Life, FP7, ekspert American Thoracic Society, liige Gruusia Teadusfond, ekspert Eur. Respir. J, Clinical Chem. Acta, retsensent J Proteomics, retsensent
Kaiu Prikk	-	European Respiratory Society, liige
Peeter Ross	-	European Society of Radiology, liige Finnish Society of Telemedicine and eHealth, liige
Madis Tiik	-	Finnish Society of Telemedicine and eHealth, liige
Kalev Karu	-	International Society of Quality in Health Care, liige
Priit Kogerman	-	EK Innovatiivse Meditsiini Initsiatiiv, rahvuslik esindaja
Vahur Valvere	-	Euroopa Meditsiinilise Onkoloogia Ühing (ESMO), liige Breast Cancer International Research Group, liige American Society of Clinical Oncology, liige
Hanna-Kaarina Pohjonen	-	UEMS eHealth Working Group, liige
Thomas Fehniger	-	Euroopa Proteomics Assotiation, special editions editor on Clinical Proteomics The American Chemical Society, special editor J Proteome Research, editor
György Marko-Varga	-	Board member of the Swedish Academy of Pharmaceutical Society, Drug Analysis Section Initiated the Swedish Proteomic Society (SPS) and currently the President President of European Proteomics Association "EuPA" International Society for Translational Medicine Faculty Member HUPO HPP Chromosome Initiative Co-Chair Swedish representative "Imaging Mass Spectrometry New Tools for Healtcare Research" European Union Member of the Advisory Board "Comprehensive Analytical Chemistry Book Series, Elsevier" Member of the Editorial Board, Journal of Pharmaceutical and Biomedical Analysis, Elsevier Science Publisher Assoc. Editor (Europe) Journal of Proteome Research, American Chemical Society Member of the Editorial Board, Current Pharmaceutical Analysis, Bentham Science Publishers Member of the Editorial Board, Journal of Multiple Organ Dysfunction, Bentham Science Publisher Invited to the Editorial Board of "Respiratory and Translational Medicine", Springer Int. Science Publisher
Ave Minajeva	-	Federation of the Societies of Biochemistry and Molecular Biology, liige

2.5 Aruandeaasta tähtsamad T&A finantseerimise allikad.

MTT12	- Biomarkers Measuring Inflammation, Mobilitas Top Researcher Grant
VE430	- Measurement of airway wall thickness in COPD with identification of new biological markers in airway tissue from COPD patients, välisleping AstraZeneca RD
Lep11009	- A multicenter, open-label, dose ranging study to determine the pharmacokinetics and pharmacodynamics of mepolizumab in moderate to severe asthma subjects, Siseriiklik leping GlaxoSmithKline Eesti OÜ

Lep10121 - A randomised, double-blind, placebo -controlled, parallel-group, multicentre, dose ranging study to evaluate the efficacy and safety of Losmapimod (GW856553) tablets administred twice daily compared with placebo for 25 weeks in adults subjects with chronic obstructive pulmonary disease Siseriiklik leping GlaxoSmithKline Eesti OÜ

ETF8116 - Kasvaja metastaseerumise molekulaarsed mehhanismid: optilised kuvamismeetodid teadaolevate ja uudsete molekulide rollide selgitamiseks Eesti Teadusfond

F12022 - "Novel MRM diagnostics pre-study", EAS eeluuringuprojekt

2.6 Soovi korral lisada aruandeaastal saadud T&A-ga seotud tunnustusi (va punktis 2.3 toodud tunnustused), ülevaate teaduskorralduslikust tegevusest, teadlasmobiilsusest ning anda hinnang oma teadustulemustele.

KMI töötajad seisuga 31.12.2011 ja nende osalemine teadusprojektides :

Isik	**Ametikoht**	**Hõive**	**Kraad**	**Kraadi tüüp**	**Osalemine projektides**
Ruth Sepper	Külalisprofessor instituudi direktor	1,0	Meditsiiniteaduste doktor, majandusmagister	PhD	VE430,VNP482, STACC, AR9082
Priit Kogerman	Professor	0,25	Filosoofiadoktor	PhD	ETF8116; V286A
Thomas Edward Fehniger	Prfessor	1,0	Filosoofiadoktor	PhD	VE430, MOTT12
Kalev Karu	Erakorraline teadur	0,5	Meditsiinikvaliteedi juhtimise magister	MQIH	AR9082, VNP429
Katrin Gross-Paju	Dotsent	0,25	Meditsiiniteaduste doktor	PhD	AR9082
Vahur Valvere	Dotsent	0,25	Meditsiiniteaduste doktor	PhD	AR9082
Kaiu Prikk	Dotsent	0,5	Meditsiiniteaduste doktor	PhD	AR9082
Kaiu Prikk	Van.teadur	0,5	Meditsiiniteaduste doktor	PhD	VE430,Lep11009, Lep10121, MOTT12
György Marko-Varga	Van. teadur	0,25	Meditsiiniteaduste doktor	PhD	VE430
Ave Minajeva	Dotsent	0,5	Meditsiiniteaduste doktor	PhD	VE430, MOTT12
Hanna Pohojonen	Dotsent	0,5	Tehnikateaduste doktor	PhD	AR9082, VNP482
Peeter Ross	Projekti koordinaator	0,6	Filosoofiadoktor (tervishoiutehnoloogia)	PhD	e-Medic
Madis Tiik	Projektijuht	0,6		MD	e-Medic
Berit Pilden	Insener	1,0	Loodusteaduse magister	MSc	MOTT12
Mariliis Sepper	Turundusspetsialist	1,0			AR9082, VNP482
Riina Blokk	Juhiabi	1,0			AR9082

Teadlasmobiilsus 2011

Ruth Sepper	direktor	Belgia	European Commission Research Directorate	13.-14.02.	koostöö
Thomas Fehniger	külalisprofessor	Taani	Lundi Ülikool, AstraZeneca	21.-30.01.	koostöö
Mariliis Sepper	spetsialist	Taani, Rootsi	Lundi Ülikool	31.01.	koosolek
Ruth Sepper	direktor	Prantsusmaa, Belgia	European Association for Bronchology and Interventional Pulmonology	9.-16.03.	kongress
Liina Parve	projektijuht	Eesti	SA Archimedes	03.02.	infopäev
Kaiu Prikk	dotsent	USA	American Thoracic Society	11.-20.05.	konverents
Liina Parve	projektijuht	Soome	Aalto Ülikool, HEMA Instituut	24.03.	koosolek
Ruth Sepper	direktor	Soome	Aalto Ülikool, HEMA	24.03.	koosolek

			Instituut		
Kaiu Prikk	dotsent	Tšehhi	GlaxoSmithKline	10.-12.04.	koosolek
Ruth Sepper	direktor	Belgia	Research Executive Agency	25.-29.04.	sõltumatu ekseprt
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	18.05.	koosolek
Ruth Sepper	direktor	Belgia	European Commission	23.-24.05.	koosolek
Thomas Fehniger	külalisprofessor	Taani, Rootsi	Lundi Ülikool, AstraZeneca	8.-19.06.	koostöö
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	12.07.	koosolek
Ruth Sepper	direktor	Taani, Rootsi	Lundi Ülikool	26.-27.08.	koosolek
Ruth Sepper	direktor	Belgia, Soome	European Commission FP/7 Specific Programme Committee theme Health1, Aalto Ülikool	4.-6.09.	koosolekud osalemine
Ruth Sepper	direktor	Belgia	Research Executive Agency	9.-14.10.	hindamis-protseduuris osalemine
Ruth Sepper	direktor	Belgia	Research Executive Agency	23.-28.10.	hindamis-protseduuris
Thomas Fehniger	külalisprofessor	Hiina	International Society for Translational Medicine	19.-26.10.	konverents
Peeter Ross	koordinaator	Läti	Turku University of Applied Sciences, Paul Stradins Clinical University Hospital	12.-13.10.	koosolek
Madis Tiik	projektijuht	Läti	Turku University of Applied Sciences, Paul Stradins Clinical University Hospital	12.-14.10.	koosolek
Ruth Sepper	direktor	Eesti	SA Archimedes	19.10.	komisjon
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	11.11.	koosolek
Ruth Sepper	direktor	Belgia	Euroopa Komisjon	8.-11.11.	koosolek
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	17.11.	koosolek
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	22.11.	koosolek
Thomas Fehniger	külalisprofessor	Taani, Rootsi	Swedish Academy of Pharmaceutical Sciences	24.-30.11.	sümpoosion
Madis Tiik	projektijuht	Soome	Turun ammattikorkeakoulu	7.-9.12.	koosolek, seminar
Peeter Ross	koordinaator	Soome	Turun ammattikorkeakoulu	7.-9.12.	koosolek, seminar
Hanna Pohjonen	dotsent	Eesti	E-Tervise SA	16.-17.12.	koosolek

2011.a toimus arvukalt erinevate teadusprojektide töögruppide arenduskoosolekuid.

17.-18. oktoobril 2011.a toimus kliinilise meditsiini instituudis Mobilitase teadusseminar, mille raames esines prof. György Marko-Varga loenguga „The Impact of BioBanking on Healthcare and Drug Developments“.

2.7 Teadus- ja arendustegevuse teemade ja projektide nimetused *(Eesti Teadusinfosüsteemi, edaspidi ETIS, andmetel)*

- Haridus- ja Teadusministeerium

sihtfinantseeritavad teemad:

- SF0140027s07, Biosignaalide interpreteerimine meditsiinitehnikas, Fridolin Ivo

baasfinantseerimise toetusfondist rahastatud projektid (sh TTÜ tippkeskused):

- B618, Elektroni-Tuuma magnetresonants (ENMR), Ago Samoson

riiklikud programmid:

- Teiste ministeeriumide poolt rahastatavad riiklikud programmid:

- Uurija-professori rahastamine:

- SA Eesti Teadusfond

grandid:

- ETF7506, Optilise koherentse fotodetekteerimise kasutamine ateroskleroosi varajasel diagnoosil, Meigas Kalju
- ETF8116, Kasvaja metastaseerumise molekulaarsed mehhanismid: optilised kuvamismeetodid teadaolevate ja uudsete molekulide rollide selgitamiseks, Kogerman Priit
- ETF8621, Uudne optiline meetod ureemiliste toksiinide - alatoitumuse ja kroonilise põletiku ning SVH riski potentsiaalsete markerite, monitooringuks, Ivo Fridolin

ühisgrandid välisriigiga:
järeldoktorite grandid (SA ETF ja Mobilitas):
tippteadlase grandid (Mobilitas):

- MTT68, Microwave and Scale enhanced NMR of Micro-Drops, -Leaflets, Cells and Nanoparticles, Witter Raiker
- MTT12, Põletiku biomõõtikud, Fehniger Thomas

- Ettevõtluse Arendamise SA

eeluuringud:
arendustoetused:

- SA Archimedesega sõlmitud lepingud

infrastruktuur (nn „mini-infra“, „asutuse infra“):

- AP027, Biosignaalide interpreteerimine meditsiinitehnikas, Ivo Fridolin

Eesti tippkeskused:

- TAR8077DB, Integreeritud elektroonikasüsteemide ja biomeditsiinitehnika tippkeskus, Ivo Fridolin

riiklikud programmid:
muud T&A lepingud:

- SA Keskkonnainvesteeringute Keskusega sõlmitud lepingud:

- Siseriiklikud lepingud:

- Lep10121, Randomiseeritud, topeltpime, platseebokontrollitud, paralleelsete rühmadega mitmekeskuseline erinevate annustega uuring, et hinnata losmapimodi (GW856553) 2xpäevas manust. tabl. tõhusust ja ohutust võrreld. platseeboga 24 näd. jooksul KOK täiskasvanu, Prikk Kaiu
- Lep11009, Mitmekeskuseline, avatud, annuseid võrdlev uuring selgitamaks intravenoosselt ja subkutaanselt manustatava mepolizumabi farmakokineetikat ja farmakodünaamikat astmahaigetel täiskasvanutel, kellel on tõusnud eosinofiilide tase veres, Prikk Kaiu
- STACC, Biomeditsiiniliste andmete integratsiooni ja kaeve KOK varaseks diagnoosimiseks, Ruth Sepper.

- <u>EL Raamprogrammi projektid:</u>

- VFP412, EuroMagNet II-A coordinated approach to access, experimental development and scientific exploitation of all European large infrastructures for high magnetic fields, Samoson Ago
- VFP413, Enhancing Access and Services To East European users towards an efficient and coordinated pan-European pool of NMR capacities to enable global collaborative research and boost technological advancements (EAST-NMR), Samoson Ago

- <u>Välisriiklikud lepingud:</u>

- V511, Autonomy preferences, risk knowledge and decision making performance in multiple sclerosis patients, Gross-Paju Katrin
- VE430, Measurement of airway wall thickness in COPD with identification of new biological markers in airway tissue from COPD patients, Sepper Ruth
- VIR523, Work Ability and Social Inclusion, Meigas Kalju

2.8 Struktuuriüksuse töötajate poolt avaldatud sihtfinantseeritava teadusteema taotlemisel arvestatavad eelretsenseeritavad teaduspublikatsioonid *(ETIS klassifikaatori alusel 1.1, 1.2, 1.3, 2.1, 2.2, 3.1, 3.2, 3.3, 4.1 ja 5.1).*

<u>1.1</u>

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Kaldmäe, Margit; Zilmer, Mihkel; Viigimaa, Margus; Zemtsovskaja, Galina; Tomberg, Karel; Kaart, Tanel; Annuk, Margus. (2011). Cardiovascular disease risk factors in homeless people. Upsala Journal of Medical Sciences, 116, 200 - 7.

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Putku, M.; Kepp, K.; Org, E.; Sõber, S.; Comas, D.; Viigimaa, M.; Veldre, G.; Juhanson, P.; Hallast, P.; Tõnisson, N.; Shaw-Hawkins, S.; Caulfield, M.J.; Khusnutdinova, E.; Kožich, V.; Munroe, P.B.; Laan, M. (2011). Novel polymorphic AluYb8 insertion in the WNK1 gene is associated with blood pressure variation in Europeans. Human Mutation, 32(7), 806 - 814.

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1.2

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1.3

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2.1

2.2

3.1

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3.2

Lauri, K.; Arund, J.; Holmar, J.; Tanner, R.; Luman, M.; Fridolin, I. (2011). Optical Dialysis Adequacy Monitoring: Small Uremic Toxins and Contribution to UV-Absorbance Studied by HPLC. Angelo Carpi, Carlo Donadio and Gianfranco Tramonti (Toim.). Progress in Hemodialysis - From Emergent Biotechnology to Clinical Practice (143 - 160).InTech - Open Access Publisher

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3.3

4.1

5.1

2.9 Struktuuriüksuses kaitstud doktoriväitekirjade loetelu *(NB! struktuuriüksus lisab struktuuriüksuse töötaja juhendamisel mujal kaitstud doktoriväitekirjade loetelu)*

Peeter Ross, TTÜ Tehnomeedikum, kliinilise meditsiini instituut
Teema: *Data Sharing and Shared Workflow in Medical Imagin* (Jagatud andmebaasid ja töövood piltdiagnostikas)
Juhendaja: prof Ruth Sepper, kaasjuhendaja prof. Hanna Pohjonen
Kaitses: 16.12.2011
Omistatud kraad: filosoofiadoktor (tervishoiutehnoloogia)

2.10 Struktuuriüksuses järeldoktorina T&A-s osalenud isikute loetelu *(ETIS-e kaudu esitatud taotluste alusel)*

2.11 Struktuuriüksuses loodud tööstusomandi loetelu

EE201100002
Meetod ja seade raskestidifundeeruvate ureemiliste jääkproduktide elimineerimise monitooringuks UV neelduvusega dialüüsil
Taotlus esitatud: 14.01.2011
Autorid: Fredrik Uhlin, Jana Jerotskaja, Ivo Fridolin
Omanik: TTÜ
Asutus: ND

EE201100016

Meetod ja seade kardiovaskulaarsete parameetrite varieeruvuse pikaajaliseks monitoorin-guks ambulatoorselt registreeritud elektrokardiogrammi ja pulsilaine signaalide baasil
Taotlus esitatud: 09.03.2011
Autorid: Kalju Meigas, Mart-Rein Rosmann, Jaanus Lass, Jüri Kaik, Kristjan Pilt, Deniss Karai, Indrek Raig, Avo Tölpt
Omanikud: Tensiotrace OÜ, TTÜ
Asutus: ND

EE201100034
Meetod allergiariskiga seotud raku kindlaksmääramiseks.
Taotlus esitatud: 11.05.2011
Autorid: Svetlana Sergejeva, Jekaterina Budarova, Maie Jürisson, Kaja Julge
Omanik: TTÜ
Asutus: ND

WO2011147425A1 (PCT/EE2011/000005)
Optiline meetod ja seade kvantitatiivseks uurea ja kreatiniini mõõtmiseks bioloogilistes vedelikes
Taotlus esitatud: 27.05.2011
Autorid: Ivo Fridolin, Jana Holmar, Kai Lauri, Merike Luman
Omanik: TTÜ
Asutus: ND

WO2012000521A1 (PCT/EE2011/000008)
Optiline meetod ja seade keskmise suurusega ja valkudega seotud ureemiliste toksiinide määramiseks bioloogilistes vedelikes
Taotlus esitatud: 28.06.2011
Autorid: Ivo Fridolin, Fredrik Uhlin, Jana Holmar, Risto Tanner, Jürgen Arund
Omanik: TTÜ
Asutus: ND

PCT/EP2011/059905
Meetod ja seade kardiovaskulaarsete parameetrite varieeruvuse pikaajaliseks monitoorin-guks ambulatoorselt registreeritud elektrokardiogrammi ja pulsilaine signaalide baasil
Taotlus esitatud: 15.06.2011
Autorid: Kalju Meigas, Mart-Rein Rosmann, Jaanus Lass, Jüri Kaik, Kristjan Pilt, Deniss Karai, Indrek Raig, Avo Tölpt
Omanikud: TTÜ, Tensiotrace OÜ
Asutus: ND

2. Struktuuriüksuse infrastruktuuri uuendamise loetelu

- Ultraheliaparaat MyLab 40,26.01.2011,25 501 €
- Mass-spektromeeter MicroTOF-Q,28.02.2011,169 686 €
- Kõrgsurve vedelik-kromatograaf,28.02.2011,50 809 €
- Optiline töölaud,7.12.2011,4 650 €
- Laser LSTP-1010-230V,15.12.2011,5 184 €
- Laseri kontroller LDKIT 1.5A-,15.12.2011,3 004 €
- Külmkapp -86 C,30.12.2011,7 600 €