A COMPUTATIONAL MODEL OF CHEMICAL AND MECHANICAL PLATELET ACTIVATION AND AGGREGATION

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Plenary Lectures

PL111

NEUROENGINEERING CHALLENGES IN NEUROSURGERY

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Neuroengineering is a research area where engineering skills are used to solve basic and clinical problems in neuroscience. The aim of the presentation is to give an insight into neuroengineering applied in neurosurgery.

Deep brain stimulation (DBS) is a method for reducing symptoms in movement disorders as Parkinson's disease and essential tremor. A thin electrode is surgically implanted with stereotactic technique at a well-defined brain structure. Our research focus on support systems for improving the surgical implantation procedure, and to increase the understanding of the DBS mechanism. A method for performing patient-specific simulations of the electric field around a DBS lead and map the data to the anatomy has been developed. The goal is to create improvement and side-disorder maps for the most common symptoms and brain targets used in DBS.

Optics is another core area we apply in neurosurgery. Several optical probe systems for intraoperative guidance have been developed. Forward-looking probes can act as "vessel alarm" by recording the tissue's microcirculation with laser Doppler flowmetry during creation of the brain trajectories in relation to stereotactic neurosurgery. In DBS this method has been evaluated in the clinical setting in more than 100 implantations. For brain tumor biopsies the method is presently introduced in combination with 5-ALA fluorescence measurements at the tumor border. 5-ALA induced fluorescence spectroscopy- and microscopy can also be used together in brain tumor surgery. Under the neurosurgical "blue-light" microscope, a hand-held probe supports the surgeon by enhancing malignant tissue. Another challenge is optical monitoring of cerebral microcirculation in the neuro-intensive care setting. A prerequisite for successful project outcome is a close collaboration between biomedical engineers and neurosurgeons. difference.

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PL211

IMAGE BASED, PATIENT SPECIFIC MEDICAL DEVICE SOLUTIONS

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Patient-specific anatomies can be reconstructed with a precision of approximately 0.5mm, using state of the art imaging modalities. This refers both to hard and soft tissues, hence with applications in clinical domains such as orthopedics, dentistry, cardiovascular surgery. Datamining techniques such as statistical shape modeling support the generation of biofidelic computer models.

However, these models have to be fed with accurate data to reflect not only the geometry but also the material properties, the loading conditions and the interface between implants and bone in case of prosthetic reconstruction. The challenge is to optimize the interface between host tissue and implant in order to achieve maximum long-term functionality, but this optimization is also dependent on the optimization of the interfacing between the implant, the surgeon and the host tissue. Thus also the surgical technique will benefit from engineering support.

Biomedical engineering is a key player to achieve this. A good geometric fit between implant and host tissue will ensure optimal initial stability. Patient-specific implants can ensure this stability, incorporating solid and porous structures where needed. Pre-operative computer assisted planning allows to optimize the surgical intervention, incorporating patient-specific biomechanical models to predict the functional outcome of the surgical intervention. And finally, in order to achieve that the pre-operative plan is accurately transferred into the surgical practice, computer assisted surgery enabled by e.g. navigation, robotics of patient-specific surgical instrumentation (guides and implants) can come into play.

Key to all state of the art developments in computer assisted surgery is the engineering on anatomy, enabled by multifunctional softwares and 3D printing technologies. Biomechanical modeling allows for patient-specific outcome prediction after surgical interventions and should become a routine practice in patient treatment. Patient specific surgical instrumentation is able to assist in realising the plan with sub-millimeter precision. Finally, quantification of the uncertainties that are inherent to biomechanical modeling is an essential contribution to reliable patient-specific outcome prediction.

Oral Presentations

ECMO - From Modelling to Clinical Trial

O111

HYDRAULIC CHARACTERISTIC OF A MIXED FLOW BLOOD PUMP FOR AN INTRACORPOREAL MEMBRANE OXYGENATOR

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Objectives: A mixed flow blood pump with an outer casing diameter of 9 mm is proposed as part of an intracorporeal membrane oxygenator. The

easy to integrate into the recirculation loop and can be adjusted continuously. In-vitro blood trials revealed lower hemolysis for the new resistance compared to the current gold standard.

Discussion: Extracorporeal continuous flow blood pumps with transfemoral cannulation work against high pressure at low flow. Up to now, hemolysis evaluation of the pumps is biased by hemolysis caused by the flow loop resistance. Our newly designed resistance causes less hemolysis, thus allowing for more meaningful and reliable hemolysis test results.

O254

A COMPUTATIONAL MODEL OF CHEMICAL AND MECHANICAL PLATELET ACTIVATION AND AGGREGATION

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Objectives: Thrombotic deposition is a major consideration in the development of implantable cardiovascular devices. Recently, it has been demonstrated that fluid mechanical shear micro-gradients play a critical role in thrombogenesis. The goal of the present work is to develop a predictive computational model of platelet activation and deposition that can be used to assess the thrombotic burden of cardiovascular devices. We have developed a comprehensive model of platelet-mediated thrombogenesis which includes platelet transport in the blood flow, platelet activation induced by both agonists generated at sites of vascular injury and shear micro-gradients, kinetics and mechanics of platelet adhesion, and changes in the local fluid dynamics due to the growth of a thrombus.

Methods: A 2D computational model was developed using the multiphysics finite element solver COMSOL 5.3a. The model can be described by a coupled set of convection-diffusion-reaction equations, and it comprises 7 species: resting and activated platelets, agonists that induce thrombosis, and an anticoagulant agent. Platelet adhesion at the surface was modeled *via* flux boundary conditions. Using a moving mesh for the surface, thrombus growth and consequent alterations in blood flow were modeled. In the case of a stenosis, the notions of shear stress-induced platelet activation in the acceleration zone and platelet deposition in the expansion zone downstream of the stenosis were studied.

Results: The model provides the spatial and temporal evolution of thrombosis in the flow field. The computed density of platelets adherent to the surface was validated against experimental data. The results confirm the importance of considering both mechanical and chemical activation of platelets.

Discussion: The developed model represents a potentially useful tool for the optimization of the design of the cardiovascular device flow path.

Acknowledgements: The present work was supported in part by the startup Corwave.

O255

ARTIFICIAL GENERATION OF SHEAR INDUCED THROMBI FOR MODELLING OF LVAD PUMP THROMBOSIS

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Objectives: Ventricular assist devices are a commonly used therapy for end stage heart failure patients. Pump thrombosis is one of the most common problems in patients supported by an LVAD. Two types of thrombus can be distinguished: white thrombi and red thrombi. The only available option to combat a PT is a lysis therapy or a pump exchange. The objective of the presented study is to develop a relevant white pump thrombus model to promote development of these concepts.

Methods: We developed an in vitro mock circulation system. The artificial blood circulation is provided by a HVAD. The HVAD pumps 80ml of human blood through the silicone loop. Parameters for inducing the white thrombus are high shear stress (4000 revolutions per minute), a rougher surface of the rotor, and an added activator of the intrinsic coagulation cascade. After two hours, the HVAD-system was checked for a white thrombus. Generated thrombi were stored for subsequent analysis (scanning electron microscopy and mechanical stability).

Results: Thrombus generation was reproducible in number and geometry. After ten test runs, 23 thrombi were detected. All these generated thrombi had a minimal size of 12 mm^2. The developed thrombi are very similar in structure compared to white patient thrombi explanted in clinic. The scanning electron microscope showed a fibrin net on the surface of all tested thrombi (n=5). All tested thrombi samples (n=5) resist high strength (max. 1.029 MPa) in compression tests, which is typical for white PT.

Discussion: The size of the thrombus should be increased for special investigational needs. A protocol was developed for reproducible and reliable production of white, shear induced thrombi for lysis therapy investigations. In addition, the similarity (biological structure, mechanical stability) to explanted patient thrombi was shown. However, additional analyses should be performed for further characterization of the artificial thrombi.

O256

FLUID-STRUCTURE INTERACTION DURING EX VIVO PLATELET PRODUCTION

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Objectives: Ex vivo platelet production in microfluidic bioreactors is a promising alternative to platelet donation for transfusion therapy. Platelets are formed by fragmentation of large bone marrow cells called megakaryocytes (MK). Hydrodynamic forces play a major role in the formation of platelets. In this work, we design microfluidic chips where isolated MK are exposed to hydrodynamic forces and we characterize their elongation and fragmentation.

Methods: Polydimethylsiloxane chips are fabricated using standard soft lithography protocols and sealed to a glass slide. The 50 µm deep rectangular chambers contain rows of 30 µm-wide adhesive pillars. Human CD34+ cells isolated from umbilical cord blood are differentiated in vitro for 12 days to yield mature MK and infused with a concentration of $2x10^5$ /mL into the chips at a wall shear rate of $1800s^{-1}$. Their elongation and fragmentation is monitored by videomicroscopy. Images were analysed using ImageJ.

Results: We perform a spatio-temporal analysis of MK elongation and show that platelet release is always preceded by a remodeling of the cell that spans over about 20 minutes, followed by a local, sudden increase in elongation velocity (5-fold increase in the 10 seconds prior to fragmentation). The amplitude of these variations is much larger than the spatial and temporal variations in the surrounding flow field.

Discussion: Earlier studies have shown that dynamic conditions for in vitro platelet production not only accelerates the process but also enhances the quality of released platelets. Here, we show that MK