coronary artery disease and adverse cardiovascular outcome. Coronary artery disease is often silent or may present with atypical symptoms due to autonomic neuropathy and therefore, many patients with minimal or no symptoms remain at high risk. The aim of this review is to discuss the role of cardiovascular imaging modalities in the diagnosis and risk stratification of coronary artery disease in diabetic patients.

Methods: We reviewed current literature of original studies on diagnosis and risk stratification of coronary artery disease in diabetic patients by stress and anatomical non-invasive imaging.

Results: In patients who are able to exercise, a normal stress echocardiogram identifies patients at low risk. The pattern of multi-vessel abnormality is associated with a dramatic increase in cardiac events with approximately a third of these patients developing cardiac death and non-fatal myocardial infarction within a few years after the test. Myocardial contrast imaging during dobutamine stress test is a promising tool and offers improved sensitivity at submaximal heart rate and allows incremental risk assessment.

Myocardial perfusion imaging with radionuclide techniques is widely used and has a well established diagnostic and prognostic value. However, even after a normal study, diabetic patients remain at higher of cardiac events compared to non diabetic patients with a normal imaging study. The low risk warrantee period after a normal imaging study is shorter in diabetic versus non diabetic patients which necessitate closer follow up of high risk patients. Coronary calcium scoring is useful in detecting early phase of atherosclerosis and provides objective information to predict cardiac events.

CT angiography may serve as a gate keeper for invasive angiography with a high sensitivity in patients with equivocal or non-feasible stress test. Prognostic value is established, but information is largely influenced by early revascularization. Limitations include artifacts, irradiation and risk of contrast nephropathy.

Conclusions: In patients with diabetes mellitus, a comprehensive assessment of the advantages and limitations of stress and functional imaging techniques can provide guidance for risk stratification, implementation of aggressive preventive therapy and selection of those who may benefit from coronary revascularization.

## P5.060
## ACTIVATABLE MAGNETIC RESONANCE NANOSENSOR AS A POTENTIAL IMAGING AGENT FOR DETECTING AND DISCRIMINATING THROMBOSIS

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Objective: The early detection and accurate characterization of life-threatening diseases such as cardiovascular disease and cancer are critical to the design of treatment. Knowing whether or not a thrombus in a blood vessel is new (fresh) or old (constituted) is very important for physicians to decide a treatment protocol. Non-invasive differentiation between old and fresh thrombi would be of clinical importance to estimate the risk for embolization and the necessity of anticoagulation.

Methods: We have designed smart MRI nano-sensors that can detect, sense and report the stage or progression of cardiovascular diseases such as thrombosis. The nanosensors were functionalized with fibrin-binding peptide to specifically target thrombus and were also labelled with fluorescence dye to enable optical imaging.

Results: We have demonstrated that our nanosensors were able to switch between T1 and T2 signal depending on thrombus age or the presence or absence of thrombin at the thrombus site. The nano-sensor exhibits T2 effect in the absence of thrombin (dark signal), while it shows T1 effect in the presence of thrombin (bright signal). Since thrombin enzyme is only present in the fresh/new thrombi and absent in the old/aged ones, the nano-sensor is activated by thrombin and shows T1 effect on the fresh thrombi while it is non-activated and shows T2 effect on the old ones.The developed nanosensors appeared to be non-toxic when tested with Chinese Hamster Ovarian cells within the tested concentrations.

Conclusions: Our data shows that these MRI nano-sensors are able to image and distinguish between fresh and old thrombi. This is a "one stop shopping" approach where a single imaging agent can be used to identify and classify thrombus throughout the body. The potential use of these nano-sensors is beyond cardiovascular disease and can also be applied for cancer detection.
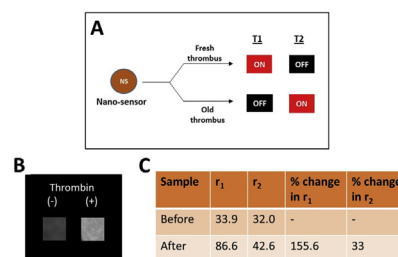


Figure 1: MRI $T_1/T_2$ switchable nano-sensors. (A) Imaging mechanism of the nano-sensor. (B) $T_1$-weighted MRI of nano-sensors in PBS in the absence and presence of enzyme thrombin. Before enzyme reaction (no thrombin), $T_1$-signal was quenched. After thrombin reaction, $T_1$ signal is restored. (C) Longitudinal relaxivity $r_1$ increased significantly (155%) after enzyme reaction while transverse relaxivity r2 changed very slightly (33%).

| Sample | $r_1$ | $r_2$ | % change in $r_1$ | % change in $r_2$ |
|---|---|---|---|---|
| Before | 33.9 | 32.0 | - | - |
| After | 86.6 | 42.6 | 155.6 | 33 |

## P5.061
## TREATMENT OF VERY PRETERM PREECLAMPSIA VIA HEPARIN-MEDIATED EXTRACORPOREAL LDL-PRECIPITATION APHERESIS: THE FREIBURG PREECLAMPSIA H.E.L.P.-APHERESIS STUDY

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Objective: The anti-angiogenetic factor soluble Fms-like tyrosine kinase-1 (sFlt-1) is causative in the pathogenesis of preeclampsia (PE) and specific removal of sFlt-1 via dextran sulfate cellulose (DSC)-apheresis was suggested as cure to allow prolongation of pregnancy in preterm PE. However, in addition a deranged lipoprotein metabolism may impact endothelial and placental function in PE. Lipoprotein-apheresis by heparin-mediated extracorporeal LDL-precipitation (H.E.L.P.) was previously applied and has been shown to alleviate symptoms in PE. This clinical trial reevaluates the clinical efficacy of H.E.L.P.-apheresis in PE considering sFlt-1.

Methods: Open pilot study assessing the prolongation by H.E.L.P.-apheresis in 6 women (30-41 years) with very preterm PE (24+4 to 27+0 gestational weeks (GW)) (NCT01967355) compared to a historic control-group matched for GW at admission (<28 GW; n=6). Clinical outcome of mothers and babies, and pre- and post H.E.L.P.-apheresis levels of sFlt-1and PlGF were monitored.

Results: In apheresis patients (2-6 treatments), average time from admission to birth was 15.0 days (6.3 days in controls; p=0.027). Lung maturation was induced in all treated cases, and all children were released in healthy condition. Apheresis reduced triglycerides and LDL-cholesterol by more than 40%. Although H.E.L.P.-apheresis induced a transient sFlt-1-peak baseline levels did not change and rather stabilized sFlt-1 levels at pre-apheresis levels throughout treatments, with sFlt-1/PLGF ratio remaining unaffected.

Conclusions: H.E.L.P.-apheresis proved again to be safe and prolongs pregnancies in PE. However, without reducing sFlt-1 levels below baseline lowering lipids or other yet undefined factors appear to be of more relevance than reducing sFlt-1.

## P5.062
## PLASMONIC PHOTOTHERMAL THERAPY OF ATHEROSCLEROSIS PROVES EFFECTIVENESS BUT NOT SAFETY FOR REAL PRACTICE: LONG-TERM SUBANALYSIS FROM NANOM-FIM

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Objective: The safety options in nanomedicine raise an issue of the optimal niche for these technologies at the real-world clinical practice. The aim of this study was to evaluate safety of the applied nanoapproach despite excellent efficacy profile with an unprecedented 30.7% reduction of plaque burden

Methods: This is an observational prospective cohort study of the five-year