S17: Rheology and Microcirculation

S17-1 Longitudinal analysis of thrombin generation biomarkers in venous thromboembolism

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Increased thrombin generation (TG) is a key mechanism in the pathogenesis of deep venous thrombosis and pulmonary embolism. In order to evaluate whether monitoring of TG could also be useful to assess the clinical course of venous thromboembolism (VTE), a prospective longitudinal analysis was performed in 354 patients (237 females, 117 males, age: 18-65 y, mean: 45.3 y) with VTE over a period of 12 months. VTE included deep venous thrombosis of the legs, pelvis, pulmonary embolism and visceral venous thrombosis. Thrombin-antithrombin-complex (TAT) and prothrombin fragment 1+2 (PTF) were assayed as biomarkers to characterize TG. Furthermore, the fibrinolytic response to thrombus formation was studied by analyzing D-dimers and plasmin-antiplasmin-complex (PAP). It could be shown that TAT was maximally elevated during the acute stage, decreasing significantly after 4 weeks, reaching lowest levels equivalent to controls not before 3-4 months, and increasing slightly after 4-12 months. This period of time was associated with the cessation of oral anticoagulation. TAT was significantly higher in recurrent thrombosis and pulmonary embolism compared to single thrombsis. The changes in PTF were analogous, but less accentuated. D-dimers showed a similar time course as TAT. This also applied, however at a lesser extent to PAP. Plasmatic viscosity and erythrocyte aggregation as hemorheologic parameters only weakly paralleled the course of TG, but were closely related to changes in fibrinogen. In conclusion, thrombin generation biomarkers, in particular TAT, are useful for monitoring the course and extent of VTE and to evaluate succesful anticoagulation. The fibrinolytic response, especially monitored by D-dimers shows a parallel time course and is therefore closely related to TG due to fibrin formation as a result. Being a highly sensitive marker, D-dimers appear even more suitable than TAT to characterize the course, extent and risk of recurrence in VTE.

S17-2 Comparison of PIRADS 3 lesions with histopathological findings after MRI-ultrasound fusion targeted biopsy of the prostate in a real-world setting

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OBJECTIVES:
We aimed to evaluate whether PIRADS 3 lesions in multiparametric MRI (mpMRI) represent a significant risk of prostate cancer (PCa) in a real-world setting of different referring radiologic institutes.

MATERIALS AND METHODS:
Between May 2015 and October 2017, a total of 408 patients were referred to our clinic for MRI-ultrasound fusion targeted biopsy of the prostate (FusPbx) due to suspected prostate cancer. In all patients, preoperatively mpMRI of the prostate was performed by altogether 62 different radiologic institutes. Prostate lesions were classified according to the PIRADS system. A PIRADS 3 lesion was diagnosed in 41 patients. FusPbx was performed transrectally using a Philips EPIQ 7 scanner with plane wise fusion of ultrasound and MRI image data. In addition to FusPbx in each patient a randomized 12-core transrectal ultrasound guided biopsy (USPbx) was performed.
RESULTS:
Mean PSA Level was 9.5 ng/ml (range: 1 – 26 ng/ml), mean patients age 66.1 years (48.6 - 80.4). In 12/41 patients (29.3 %) prostate cancer was diagnosed by FusPbx of the PIRADS 3 lesion. In the target lesion PCa was classified as Gleason Score 3+3 in 5 patients, as 3+4 in 3, 4+3 in 1, 4+4 in 1 and 4+5 in 1 patient. In patients with negative FusPbx USPbx revealed PCa in another 7 patients (17.1 %). In 5 of these GS 3+3 PCa was found, in another 2 patients GS 3+4 PCa.
CONCLUSIONS:
PIRADS 3 lesions indicate an equivocal likelihood of significant prostate cancer by definition. In our series with a large number of referring radiologic institutes, PCa detection rate was 29.3 % in PIRADS 3 lesions. This might indicate, that the definition of a PIRADS 3 lesions varies along different radiologic institutes. Quality and reproducibility of mpMRI prostate imaging might be improvable by training.

S17-3 Does acoustic radiation force Elastography help to improve the diagnostic value of ultrasound in the preoperative characterization of tumors of the parotid gland?

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Objectives:
While ultrasound is the preferred method of preoperative evaluation of masses of the parotid glands, existing methods do not allow for definite differentiation between the most common benign and malignant tumors. The aim of our study was to evaluate if acoustic radiation force with Virtual Touch Quantification (VTQ) elastography improves preoperative evaluation of parotid tumors.
Methods:
We investigated the parenchyma of 102 parotid glands, fourteen lymph nodes of healthy volunteers and 51 tumors of the parotid gland via ultrasound, color Doppler ultrasound and VTQ. Subsequently, we analyzed the results and compared with histopathology.
Results:
Perfusion was significantly lower in comparison to malignant tumors in pleomorphic adenoma, the most frequent benign tumor of the parotid gland. Furthermore, all tumors showed statistically significant higher perfusion in comparison to the parenchyma or the lymph nodes of the gland. By a statistically significant amount, the shear wave velocity of the user-defined region of interest was more frequently an overflow value higher than 8.5 m/s in total tumors in comparison to parenchyma or lymph nodes. In comparison, the different tumor types presented no significant difference in the shear wave velocity.

Conclusions:
VTQ in combination with classical ultrasound examination provides additional data that improves the ability to distinguish between benign and malignant tumors. Thus, VTQ shows promise for integration into preexisting ultrasound protocols. However, despite the improvement, even with VTQ complete differentiation of tumors is still not possible, and further investigation is recommended.

S17-4 Technologies for Adipose Stem Cell Isolation

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Background: Fat grafting has become one of the most frequent procedures in plastic surgery. High absorption rates caused by insufficient vascularization and impaired adipocyte vitality lead to unpredictable graft take rates. The proliferative and angiogenic properties of adipose tissue-derived stem cells hold great promise to overcome this problem. Therefore, strenous efforts have been made to enrich lipoaspirate with stem cells. A comparison of these studies is difficult as many parameters are influencing the results. Objective: This study summarizes the abundance of factors that influence the stem cell yield, which include harvesting, isolation and quantification. Methods: Stem cells were isolated from lipoaspirate and quantified using flow cytometry, colony forming unit assays and conventional cell counting. However, only one parameter was changed for every comparison evaluated. Results: Isolation of cells from the lipoaspirate of the same patient and harvesting site can show huge differences depending on isolation protocol details and quantification method. Discussion and Conclusion: Stem cell yield is influenced by many so factors that the comparison of different studies should be handled with care.

S17-5 Blood rheology in breast and gynecologic cancer patients at primary diagnosis and stage of cancer progression

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Background: Patients with gynecological malignancies often show increased plasma viscosity and red blood cell aggregation and a tendency of anemia at the time of primary diagnosis, resulting in an hematocrit-independent hyperviscosity syndrome. This is commonly accompanied by coagulation activation characterized by elevated platelet count and increased blood clotting factor turnover. Similar changes in the blood rheological properties were shown in patients with breast cancer that refer to a higher risk for deep vein thrombosis. An association between blood rheological properties including red blood cell deformability and RBC indices in the gynecologic cancer patents has not yet been proofed. Methods: Measurement of the rheological properties including plasma viscosity (PV), red blood cell (RBC) aggregation during stasis (E0) and low shear conditions (E1), red blood cell deformability during exposure to low (RBC 1.2, 3.0), moderate (RBC 6.0, 12.0) and high shear forces (RBC 30.0, 60.0) were performed before primary surgery and at the time of

disease progression. Results were compared to those of healthy patients, prior to elective gynecological surgeries. The rheological parameters were correlated to red blood cell indices (RBC-I: MCH, MCV and MCHC). Results: In total 44 patients with gynecological malignancies, here 12 patients with ovarian carcinoma, 13 patients with endometrium carcinoma, 13 patients with cervical carcinoma and 6 patients with vulvar cancer, 8 patients with gynecological cancer progression, 28 women with breast cancer and 19 women with progression or contralateral breast cancer participated in this study. These data were compared to those of 286 healthy women. The plasma viscosity tended to be higher in the patients with carcinoma. RBC aggregation in stasis was moderately higher in breast cancer and highest in stage of gynecological cancer progression, while RBC aggregability during exposure to low shear conditions tended to be higher in all the patients with malignancies, highest in stage of progression, in comparison to healthy women. Compared to healthy patients RBC deformability in primary breast cancer including metastatic stages and gynecological malignancies was higher. RBC deformability in vulvar carcinoma was highest compared to the other malignancies and lowest in the patients with disease progression. There was a strong inverse correlation between MCV and RBC deformability in all cancer types and stages, being most pronounced under high shear forces. Discussion: We confirm the typical constellation of blood rheological properties in the gynecologic cancer patients in the sense of a hyperviscosity syndrome. Interestingly, compared to healthy individuals, RBC deformability at primary cancer diagnosis was higher - particularly in breast cancer patients – but decreased in the presence of cancer progression.

S17-6 First experiences with an into the clinical work flow integrated CAM Assay in Patients with oral squamous cell carcinoma

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Abstract:
Introduction: The oral squamous cell carcinoma (OSCC) is a leading cause of death in human malignancies. The aim of this study is to integrate the CAM Assay as a reliable and good working in vivo model for the evaluation of OSCC tumor samples and its growth into the clinical work flow.
Material and Methods: Fresh human Tumor samples (OSCCs) 1x1mm in size were cut into 350µm thick slices by a Vibratome and put on the prepared CAM model.
After growth of the tumor tissue on the CAM we started with topical induction of proinflammatory cytokines (TNFα) and growth factors (TGFβ). After further growth of the

tumor on the assay we explanted the tumor tissue and first performed microscopic and then immunohistochemical examinations. E-cadherin and vimentin were used as EMT-makers and the histologic preparations were evaluated histomorphometrically. The results were correlated with clinical parameters of the patients.
Results: Under TNFα, the small tumors (T1 / T2) show higher E-cadherin expression than larger tumors (T3 / T4). The vimentin expression under TNFα behaved in the opposite direction, at T1 / T2 the expression decreased in T3 / T4 increased. Furthermore, an increased E-cadherin expression in N0 and diminished E-cadherin expression in N1 / N2b patients could be detected depending on the N-stage of the patients. Vimentin, on the other hand, was reduced in the N0 group and expressed more frequently in the N1 / N2b group. TGFβ induction also led to increased expression of vimentin in the T3 / T4 tumors and N1 / N2b stages.
Conclusion: By integrating a CAM assay into the clinical workflow, tumors with preserved tumor architecture can be cultured and subjected to histological and molecular biology studies. Effects on biological behavior are recognizable and demonstrable in this model. The key markers E-cadherin and vimentin alone are not sufficient to represent the complexity of the EMT in this model. Further molecular biology and signaling pathway analyzes are necessary.