

Table 2: Characteristics of flow-based assays to assess haemostasis

Assay [1]	Blood interaction surface	Incorporates shear					Use		
		complex secondary flow (vortexes, recirculation zones)	Venous	Arterial	Arteriolar	Stenotic	in vitro; with blood of	ex vivo; attached to vein outflow of	in vivo
Bleeding time [2-7]	Induced skin vessel injury	+ ?	-	+?	+				man/animal
Cone and plate analyzer [8-28]	Endothelial cell matrix, polystyrene, purified proteins	-	-	+ 1800s-1	-	-	man/animal		
Coaxial cylinder Couette- [29-40]	Particles with purified proteins, platelet activation by SIPA (shear-induced platelet activation) and/or agonists, typically ADP and TRAP (thrombin agonist)	-	100-8000 s-1				man/animal		
Annular perfusion chamber [41-48]	Human and rabbit endothelial denudated arteries and α -alfa-chymotrypsin digested rabbit arteries	50-3300 s-1					man/rabbit	man	incorporated in arterio- venous loop of rabbit
Parallel plate perfusion chamber [46-84]	Purified fibrillar collagen types 1 and 3, purified proteins, synthetic grafts and catheter materials, human tissue factor + phospholipids, human cultured vascular cells and their corresponding extracellular matrix and sections of human artery plaque material	50-10500 s-1			2600-32000 s-1	man, mouse, rat ,rabbit	man	incorporated in arterio-venous loop of dog	
Platelet aggregation in stirred PRP [73,74,85-92]	Platelet activation by added agonists: ADP, epinephrin, collagen, thrombin, von Willebrand factor or specific (engineered) receptor agonists	no clear rheologic profile: mixed shear presence (high close to the stirrer bar and low at other places)				man/animal			
Platelet agglutination [93,94]		no clear rheologic profile: mixed shear presence (high close to the stirrer bar and low at other places)				man/animal			
Platelet aggregation in stirred whole blood [74]		no clear rheologic profile: mixed shear presence (high close to the stirrer bar and low at other places)				man/animal			
Rapid Platelet Function Analyzer [17,95]	Platelet activation by protein (e.g. fibrinogen) coated beads cartridges	no clear incorporation of shear				man/animal			
Platelet function analyzer (PFA)-100 [7,73,74,85,96-113]	Collagen /epinephrin and collagen/ ADP cartridge	-	-	+ 5000-6000 s-1	+	+/-	man/animal		

Assay	Blood needed	Evaluation of haemostasis and thrombus formation					Evaluation of fibrin formation
		Adhesion	Aggregation	Release	Receptors	Procoagulant activity	Coagulation factor activation to fibrin
Bleeding time	< 1-2 ml/assay	+ general but not discriminating test for platelet vessel wall interactions					-?
Cone and plate analyzer	0.2 ml/ assay	+	+	+	dependent on the used interaction surfaces	-?	-?
Coaxial cylinder couette-	200-400 µL/ assay	of platelets, or other blood cells to protein-coated beads	after SIPA, and/or after agonist (ADP and TRAP) stimulation	direct measures from aliquots post-shear and indirect by markers for secretion by flow cytometry	sensitive for GPIb, GPIIb/IIIa, deficiencies and dysfunction;	potential sensitivity and markers by flow cytometry, including microparticle analyses	potential measures of fibrin formation via fluorescent labelled fibrinogen and flow cytometry, or via activation markers
Annular perfusion chamber	10-50 ml/min (usually 30-50 ml/ assay)	radio and fluorescent, labelled platelets, en face morphometry of thrombus sections, standard morphometry and computer-assisted morphometry and confocal microscopy of thrombus coverage, and blood flow measurements.	morphometry as indicated for "Adhesion" and immunologic assessment of platelets and fibrin of plasmin digested thrombi	sensitive for ADP and TxA2 release β-TG and selectin in plasma. Flow cytometry of activated platelets with PAC-1 and annexin V and platelet micro-particle formation	sensitive for GPIa, GPIb, IIb/IIIa, VI, deficiencies and dysfunction, also ADP receptors. Scott syndrome, Stormorken syndrome, deficiencies of FVII, FVIII, FIX, FXI, FXII and fibrinogen, Protein C and, FV Leiden	+ in case of non anticoagulated in vivo/ ex vivo perfusions and in vitro LMWH anticoagulated blood, detection of phosphatidyl serine exposure. Assessment of plasma FPA, TAT and F1+2	Fibrin deposition after in vivo, ex vivo and in vitro with LMW heparin anticoagulated blood perfusions. Measured by morphometry as indicated for "Adhesion". Fluorescence labelling of fibrinogen
Parallel plate perfusion chamber	5-50 ml/min (usually 30-50 ml / assay); with miniaturized chambers 3-5 ml / assay often suffices						
Platelet aggregation in stirred platelet rich plasma	?	-		+	dependent on agonist specific responses	+	-
Platelet agglutination	?	mediated by GPIb/ VWF interaction	-		mediated by GPIb	-	-
Platelet aggregation in stirred whole blood	?	-	+	+	dependent on agonist specific responses	-	-
Rapid Platelet Function Analyzer	< 1ml /assay		+	Possible	beads cartridges for testing the efficacy (dosing) of specific platelet activation inhibiting drugs	-	-
Platelet function analyzer (PFA)-100	?	+ collagen/epinephrin vs collagen/ ADP cartridge	+ collagen/epinephrin vs collagen/ ADP cartridge	+ collagen/epinephrin vs collagen/ ADP cartridge	- Collagen/epinephrin vs collagen/ ADP cartridge	-	-

FPA= fibrinopeptide A, TAT = thrombin antithrombin III complex, F1+2 = fragment 1+2, β-TG = beta-thromboglobulin, TxA2 = thromboxane A2, GP = glycoprotein, VWF = von Willebrand factor, TRAP = Thrombin Receptor Activating Peptide