Thromboembolic complications have been identified as the second most common cause of death in breast cancer patients [1,2]. The interaction and result thereof, between circulating tumour cells and platelets is complex and reciprocal: platelet activation and aggregation has been implicated in facilitating coagulation-mediated metastasis; tumour-derived cytokines and growth factors have been implicated in thrombocytosis [3] and malignancy itself is associated with increased risk of thromboembolism [1,2]. Platelet and fibrin network morphology is altered in human disease conditions such as diabetes, stroke and cancer and associated with thrombosis [4,5]. It is thus understood that the in vivo relationship between breast cancer cells and platelets may lead to changes in platelet morphology and function, increasing susceptibility to thrombosis.

The reciprocal interactions between tumour cells and coagulation ability in vitro were investigated, by assessing ultrastructural alterations in platelet and fibrin network morphology, through the establishment of a co-culture system (MCF-7 luminal phenotype breast cancer cells cultured with blood plasma of healthy female individuals). Co-cultures were implemented for 5 to 30 min after which platelet and fibrin network coagula were prepared as per published protocol [5] on glass coverslips.

Utilising scanning electron microscopy, we found that enhanced fibrin network formation and platelet aggregation appears to take place concurrently [6,7]. Changes in morphology from normal were visible as early as 5 min in co-culture, with platelets displaying pseudopodia extension and fibrin networks increasing in density. At 10 and 15 min, distinguishable morphology deteriorated drastically, with platelets spreading their hylomeres and fibrin plaque formation. By 20, 25 and 30 min there was almost no semblance of normal characteristics in both platelet and fibrin network preparations, with dense plaque formation in both. This induced deterioration of cellular and fibre characteristics resembles that of previously studied blood plasma preparations of severe inflammation- and thrombosis- prone patients [4,5].

In conclusion, our preliminary results seem to indicate that the in vitro environment closely mimics the in vivo at an ultrastructural level, evidencing that it may indeed be the reciprocal interaction between tumour cells and the coagulation system which induces thrombosis, regardless of other systemic factors. The more rigid the construction of platelet and fibrin networks, the more impaired fibrinolysis would be. These results offer picturesque confirmation that breast cancer patients would be increasingly susceptible to thrombotic-related consequences [8].

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Fig. 1: Platelet ultrastructure. Platelet rich plasma was co-cultured with MCF-7 breast cancer cells. Ultrastructure was studied preparing platelet coagula from plasma. A: Control platelet, unexposed to cells. Experimental platelets B: 5min co-culture, C: 15min co-culture, D: 30min co-culture (Scale bar = 1µm)

Fig. 2: Fibrin network ultrastructure. Platelet rich plasma was co-cultured with MCF-7 breast cancer cells. Ultrastructure was studied preparing fibrin coagula through addition of thrombin to plasma. A: Control fibrin networks, unexposed to cells. Experimental networks B: 5min co-culture, C: 15min co-culture, D: 30min co-culture (Scale bar = 1µm)