



## **Towards Mechanical Clinical Markers in Sickle Cell Disease: Dynamics of Red Blood Cell in Low Shear Flow**

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# **Towards Mechanical Clinical Markers in Sickle Cell Disease: Dynamics of Red Blood Cells in Low Shear Flow**

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Several regimes of motion are evident in red blood cells (RBCs) under shear flow and are known to be controlled by the shear flow rate and by the deformability of the cell. Above a certain shear flow rate, healthy RBCs present a fluidized regime analogous to that of a droplet: the membrane adopts a tank-treading motion, i.e. rotates around the centre of mass of the cell, and its orientation oscillates around a mean value. This motion is not observed in rigid RBCs which keep the same regime of motion as with low shear flow rate. The transition from one motion to the other depends on several intrinsic parameters including membrane viscosity, elasticity and cytoplasmic viscosity.

Sickle cell disease (SCD) is a hereditary hemolytic anemia due to the presence of mutant hemoglobin, Hb S, which tends to polymerize in RBCs, reducing its deformability and resulting ultimately in RBC sickling. We postulate that SCD may affect RBCs capacity to adopt the tank-treading motion.

Thanks to microfluidic chips coupled with high speed video, we studied the fraction of RBCs displaying a tank-treading motion (% of TT) at moderate shear stresses (0.4-0.6 Pa), in homozygous SCD patients (n=30) and in normal subjects (n=12). At the time of sampling, SCD patients were in steady state (no vaso-occlusive crisis or other acute complications) and not transfused for at least 3 months. Around 3 microL of total blood were necessary for each measurement. RBCs were studied under atmospheric conditions and exhibited the normal discoid shape.

We showed first that the % of TT is significantly different in SCD patients compared to controls, with no overlap between the values of each groups (respectively  $70.4 \pm 12.9\%$  versus  $98.6 \pm 0.9\%$ ). Second, measurements performed on different cells fractions isolated by cell density or in the presence of different NaCl concentrations, showed that the % of TT cells is sensitive to cell density and hydration status, both in normal subjects and in SCD patients. Finally, we evaluate the % of TT in RBC samples drawn just before or during 10 episodes of vaso-occlusive crisis from 8 different patients. The definition of a vaso-occlusive crisis, for this specific study, was set as an episode with pain in at least 2 different locations requiring hospitalization at least for 24h. The results revealed that, for a given patient, the % of TT cells varies significantly for 12h before as well as during vaso-occlusive crises with kinetics comparable from one patient to another.

In conclusion, we described here a new inexpensive biological test able to discriminate healthy RBCs from sickle RBCs, with preliminary results suggesting potential interest for monitoring the clinical status of SCD patients. Further analysis will be necessary to determine if this parameter is suitable for predicting the occurrence of vaso-occlusive crises early enough to allow preventive actions.