Acta Biomaterialia 8 (2012) 4130–4138

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Optical measurement of biomechanical properties of individual erythrocytes from a sickle cell patient

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ARTICLE INFO

Article history:
Received 29 November 2011
Received in revised form 10 June 2012
Accepted 11 July 2012
Available online 20 July 2012

Keywords:
Sickle cell disease
Red blood cell
Cell biomechanics
Cell membrane
Optical measurement

ABSTRACT

Sickle cell disease (SCD) is characterized by the abnormal deformation of red blood cells (RBCs) in the deoxygenated condition, as their elongated shape leads to compromised circulation. The pathophysiology of SCD is influenced by both the biomechanical properties of RBCs and their hemodynamic properties in the microvasculature. A major challenge in the study of SCD involves accurate characterization of the biomechanical properties of individual RBCs with minimum sample perturbation. Here we report the biomechanical properties of individual RBCs from a SCD patient using a non-invasive laser interferometric technique. We optically measure the dynamic membrane fluctuations of RBCs. The measurements are analyzed with a previously validated membrane model to retrieve key mechanical properties of the cells: bending modulus; shear modulus; area expansion modulus; and cytoplasmic viscosity. We find that high cytoplasmic viscosity at ambient oxygen concentration is principally responsible for the significantly decreased dynamic membrane fluctuations in RBCs with SCD, and that the mechanical properties of the membrane cortex of irreversibly sickled cells (ISCs) are different from those of the other types of RBCs in SCD.

1. Introduction

Sickle cell disease (SCD) or sickle cell anemia is an inherited autosomal blood disorder characterized by abnormal mechanical and rheological behavior of red blood cells (RBCs). SCD is caused by sickle hemoglobin (HbS), a variant hemoglobin (Hb) molecule resulting from a point mutation in the β-globin gene [1]. Upon deoxygenation, HbS polymerizes or self-assembles inside the RBC and significantly alters and damages the cytoskeleton and membrane cortex, resulting in a sickle-shaped RBC. This sickle RBC has decreased deformability, causing abnormal rheology in sickle blood and eventually various complications of SCD: ischemia and organ damage can result when microcirculation is impeded due to the poorly deformable RBCs. As a result of these complications and the limited choices for medical treatments, life expectancy for SCD patients is short; only 50% of patients with SCD survive beyond their fifth decade [2].

Characterization of the mechanical properties of RBCs is crucial to understanding the pathophysiology of many RBC-related diseases [3–5]. While the biochemistry of HbS is well understood, the mechanical properties of individual RBCs in SCD have not been fully assessed, largely due to the limitations of the measurement techniques [6]. Studies using filtration [7] or ektacytometry [8] have revealed that the sickle RBCs are stiffer than normal RBCs. However, these techniques cannot distinguish the mechanical properties of subpopulations of sickle RBCs or isolated RBCs, and they measure properties averaged over all RBCs in a blood sample. Micropipette aspiration [9], optical tweezers [10], the parallel-plate flow chamber method [11], and atomic force microscopy [12] have been employed to study the biomechanics of SCD at the cellular level. Although these methods have significantly enhanced our understanding of sickle cell biomechanics, none of them can probe all of the key mechanical parameters of individual RBCs simultaneously. Moreover, these previous methods rely on large, quasi-static external loads or perturbations to deform sickle RBCs through physical contact, and thus are not well suited to measure mechanical properties within linear deformation regimes.

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http://dx.doi.org/10.1016/j.actbio.2012.07.011