CORRELATION BETWEEN RED BLOOD CELL MEMBRANE DECONSTRUCTIONS AND ADMINISTRATION OF EXOGENOUS ERYTHROPOIETIN IN PATIENTS ON HAEMODIALYSIS

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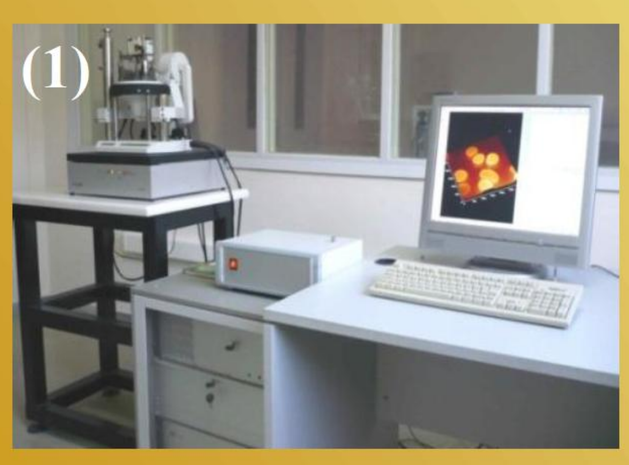
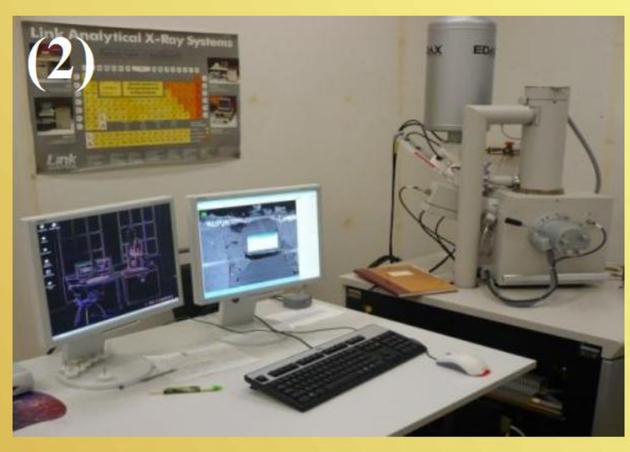
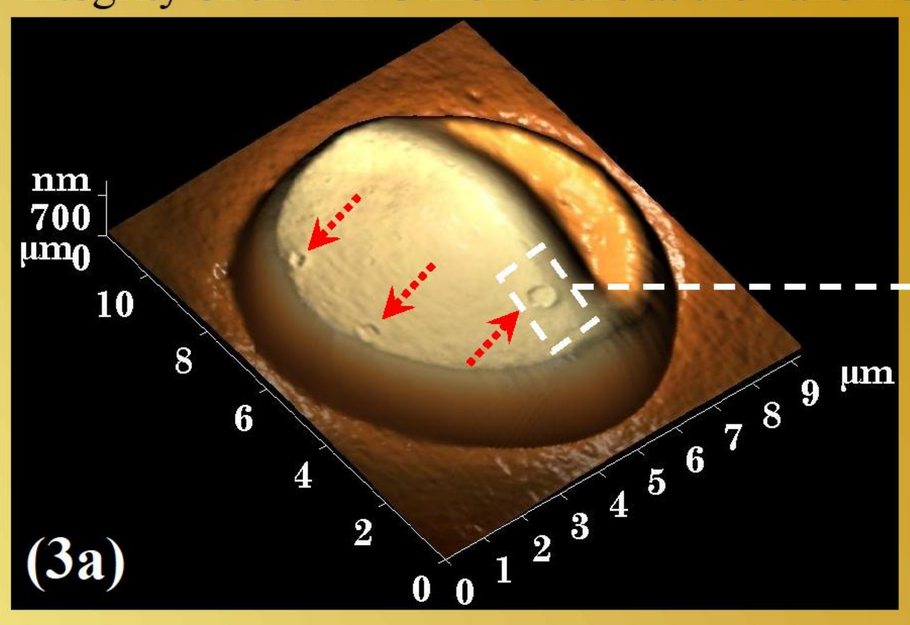
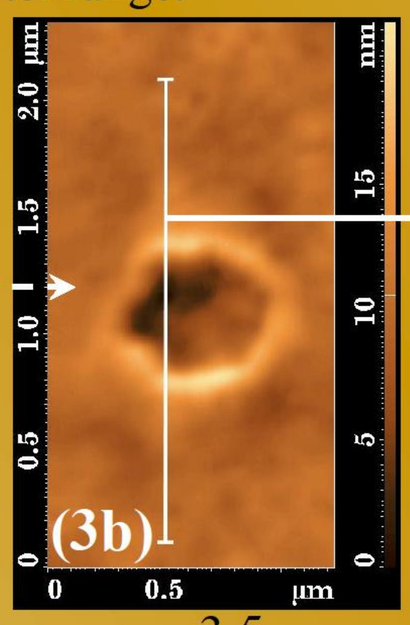
OBJECTIVES: End-stage renal disease patients on haemodialysis (HD) exhibit insufficient production of endogenous Erythropoietin (enEPO). As a consequence, they suffer from chronic anaemia that is currently treated with the administration of exogenous EPO (exEPO). However, the safety of exEPO has recently been questioned and there are no studies assessing structural integrity of the red blood cells (RBCs) produced. To address this issue, we assessed RBC membrane integrity with advanced microscopes (Figures (1)-(2)) in healthy donors and patients on HD [1-3].

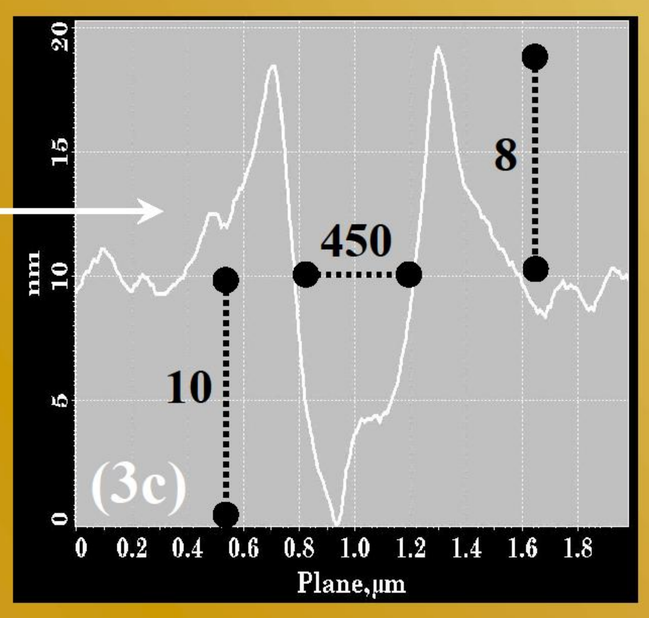
METHODS: Intact RBCs (iRBCs) of healthy donors [Group A: donors=10/iRBCs=300] and two groups of patients on HD, the first not receiving exEPO [Group B: donors=9/iRBCs=270] and the second receiving exEPO [Group C: donors=10/iRBCs=300, darbepoetin alfa (HD patients=2), epoetin alfa (HD patients=3), epoetin beta (HD patients=4) and methoxy polyethylene glycol-epoetin beta (HD patients=1): mean dose =369±171 IU/Kg/week] were studied with Atomic Force Microscope (AFM) (Figure (1)) and Scanning Electron Microscope (SEM) (Figure (2)), allowing quantitative assessment of structural integrity of the RBC membrane at the nanometer range.

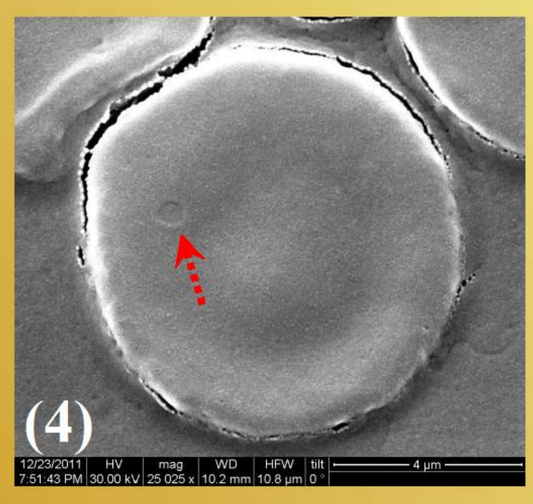




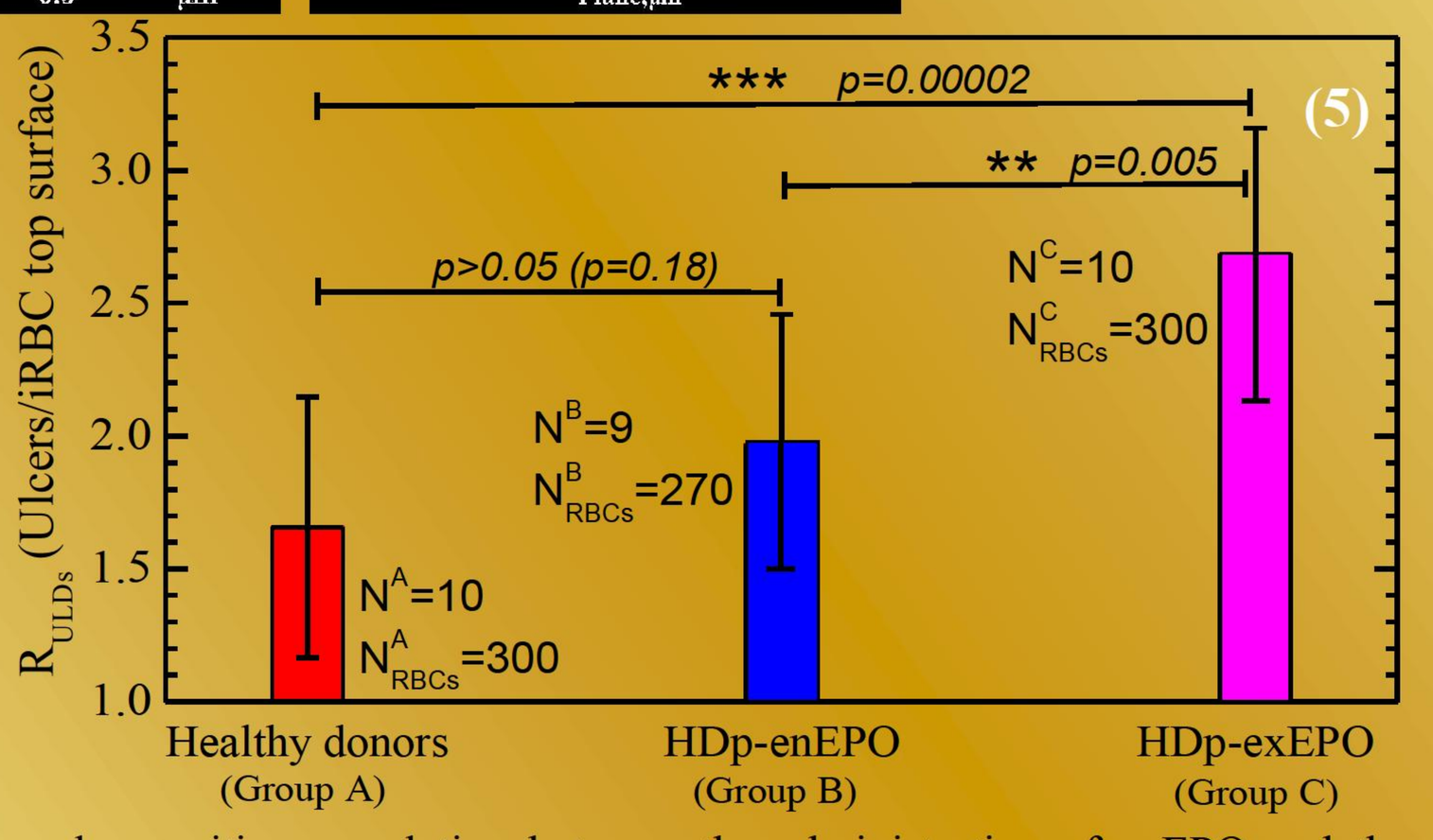








RESULTS: In all three groups there were ulcer-like deconstructions (ULDs) in the iRBC membrane, that possibly relate to physiological aging and apoptotic processes (Figures (3a)-(3c);AFM and Figure (4);SEM). Quantitatively, significant differences were observed in the mean number of ULDs detected on the top surface of iRBC membrane between the three groups: $R_{ULDs}{}^{A}$=1.66±0.49, $R_{ULDs}{}^{B}$=1.97±0.49 and $R_{ULDs}{}^{C}$=2.68±0.47. These differences were statistically significant between groups A-C (p=0.00002) and B-C (p=0.005), while between groups A-B no statistically significant difference is observed (p=0.18) (Figure (5)).



CONCLUSIONS: The present microscopy data reveal a positive correlation between the administration of exEPO and the deconstruction of the RBC membrane. This implies that exEPO, necessarily administered to HDp with lack of enEPO, probably produces RBCs with vulnerable membrane. Else, the deconstruction of the RBC membrane, as caused from a different mechanism (e.g. increased uremic milieu that however is not observed in Group C), leads to the need of exEPO administration. The present results raise serious concerns regarding the 'structural integrity' and the relevant 'biochemical parity' of RBCs produced from exEPO in respect to the ones produced from enEPO.

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M) Dialysis. M5) Anaemia in CKD 5D.

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