Proton NMR Study of the State of Water in Fibrin Gels and Blood Clots

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Blood clots and retracted (1) blood clots have been found to differ in their susceptibility to drug mediated fibrinolysis (2). The liquid component in blood clots allows for the transport of fibrinolytic drugs, yet relatively little is known about the state of water in these systems. A proton NMR relaxation and diffusion study of water in fibrin gels and blood clots has been performed with special emphasis on the effect of the shrinkage (retraction) transition.

It is shown that a measurement of the water proton T_1/T_2 ratio allows for a determination of the bound water fraction in all these systems. Proton NMR studies of gels (3,4) have established the existence of fast exchange between the water bound to the surface of the polymer network and the free water in the gel. Since the life time of a water molecule in a given phase is short compared to the spin relaxation time associated with this phase, we have a unique relaxation time characterizing protons in different environments. In order to determine the bound water fraction, the relaxation times of bound water have been estimated by an approximate procedure taking into account the intra- and intermolecular relaxation of water bound to the fibrin surface, the chemical exchange of water and fibrin protons, and cross-relaxation of bound water protons with fibrin protons. The change in the T_1/T_2 ratio at the shrinkage transition further allows for a determination of the surface fractal dimension of the gel if the change in the volume of the gel is known (5).

Our results show that the bound water fraction (η) increases from about 2.3×10^{-3} in the non-shrunken fibrin gel to about 10^{-2} in the shrunken fibrin gel where the ratio of gel volumes after and before the shrinkage transition is $V_2/V_1 = 0.13$. A smaller increase in η was observed after retraction of blood clots ($V_2/V_1 = 0.39$), η being about 1.8×10^{-2} in nonretracted blood clots and about 3.0×10^{-2} in retracted blood clots.

Even in retracted blood clots the bound water fraction remains small. This means that the overall extracellular water self-diffusion coefficient is not expected to decrease significantly even after retraction of fresh blood clots. This was indeed verified by pulsed field gradient NMR studies which showed that $D \approx D_{free}(1 - \eta) = 1.9 \times 10^{-5}$ cm^2/s. This finding suggests that the diffusion of water soluble fibrinolytic drugs into fresh thrombi is not significantly hindered by the protein polymer network.

References

1. E. Morgenstern, U. Korell, and J. Richter. Thromb. Res. **33**, 617 (1984).
2. M. Šabović and D. Keber, Fibrinolysis, Suppl. **1**, 141 (1988).
3. J.R. Zimmermann and W.E. Brittin, J. Phys. Chem. **61**, 1328 (1957).
4. F. Tabak, M. Corti, L. Pavesi, and A. Rigamonti, J. Phys. C **20**, 5691 (1987).
5. R. Blinc, O. Jarh, A. Zidanšek, and A. Blinc, Z. Naturforsch. **44a**, 163 (1989).