Fibrin fibers provide structural and mechanical integrity to blood clots and, in the process of fibrinolysis, are digested by the enzyme plasmin. Fibrinolytic therapy plays a major role in the treatment of acute pulmonary embolism and many cardiovascular diseases. However, studies have shown some clots to be resistant to fibrinolytic therapy, although the mechanisms underlying this are not clear. We are working to deconvolve the respective fibrinolytic influences of clot structure, fiber properties, enzyme kinetics, and enzyme perfusion rates into clots. Previously, we directly measured the lysis rates of individual fibers, finding that 30% of fibers lose their inherent tension during lysis and elongate rather than dissolving or being transected. This effect was independent of plasmin concentration but correlated inversely with fiber diameter: thinner fibers were more likely to lyse and fibers greater than 200 ± 30 nm in diameter more likely to elongate. We have extended these results to consider the lysis of fibers within small fibrin networks. We tracked changes in fiber morphology within a 24-hour period during lysis. Our results indicate that, within networks, > 95% of fibers elongate during lysis, and many reach a state where they become resistant to further lysis. 50% of the fibers showed no further fibrinolytic susceptibility after the first sixty minutes of plasmin exposure. Mechanisms underlying fibrin elongation will be discussed.