Intracellular ice formation (IIF), a major cause of cryoinjury in biological cells, is significantly more pronounced during freezing of tissue compared to suspended cells. While extensive studies of IIF have been conducted for single cells in suspension, few have investigated IIF in tissue. Due to the increased complexity arising from both cell-substrate and cell-cell interactions in tissue, knowledge of cryobiology of isolated cells cannot simply be extrapolated to tissue. Several theories for the mechanisms of IIF in tissue have been hypothesized, but none have been conclusively proven. Towards the goal of developing mathematical models to accurately predict the probability of IIF in tissues of one or more cell types, we have developed a novel high-speed video cryomicroscopy system capable of image acquisition at sampling rates up to 32,000 Hz. Specifically, the effects of cell adhesion and cell-cell interactions were investigated with experimental (micropatterned endothelial cell constructs) and mathematical models (Monte Carlo simulations). We have reported the first direct observation of the IIF process recorded at sub-millisecond and sub-micron resolution. In our experiments, IIF nucleation occurred preferentially at the cell perimeter. This finding was inconsistent with the commonly accepted hypotheses of ice nucleation in suspended cells and suggests an alternative mechanism of IIF initiation is dominant in adherent cells. In addition, the kinetics of ice nucleation were shown to be influenced by time in culture, attached cell perimeter, fibronectin coating density, and degree of cell-cell contact. Moreover, an additional phenomenon, paracellular ice penetration, was identified and correlated with focal adhesion formation. These studies bring closer the goal of elucidating the primary mechanisms contributing to IIF in tissue; providing important contributions to both the fields of cryopreservation (minimizing IIF) and cryosurgery (maximizing IIF).